Materials Science and Engineering C 57 (2015) 414–433

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Review

Classification, processing and application of hydrogels: A review

Faheem Ullah [a], Muhammad Bisyrul Hafi Othman [a], Fatima Javed [b], Zulkifli Ahmad [a], Hazizan Md. Akil [a,*]

[a] School of Materials and Mineral Resources Engineering, Engineering Campus, Universiti Sains Malaysia, Seri Ampangan, 14300 Nibong Tebal, Pulau Pinang, Malaysia
[b] Department of Chemistry, Quaid-e-Azam University Islamabad, 45320 Islamabad, Pakistan

ARTICLE INFO

Article history:
Received 17 February 2015
Received in revised form 23 June 2015
Accepted 25 July 2015
Available online 29 July 2015

Keywords:
Hydrogels
Crosslinked networks
Hydrogel classification
Smart hydrogels
Superabsorbent polymers
Super porous hydrogels

ABSTRACT

This article aims to review the literature concerning the choice of selectivity for hydrogels based on classification, application and processing. Super porous hydrogels (SPHs) and superabsorbent polymers (SAPs) represent an innovative category of recent generation highlighted as an ideal mould system for the study of solution-dependent phenomena. Hydrogels, also termed as smart and/or hungry networks, are currently subject of considerable scientific research due to their potential in hi-tech applications in the biomedical, pharmaceutical, biotechnology, bioseparation, biosensor, agriculture, oil recovery and cosmetics fields. Smart hydrogels display a significant physiochemical change in response to small changes in the surroundings. However, such changes are reversible; therefore, the hydrogels are capable of returning to its initial state after a reaction as soon as the trigger is removed.

Contents

* Corresponding author.
E-mail address: hazizan@usm.my (H.M. Akil).

http://dx.doi.org/10.1016/j.msec.2015.07.053
0928-4931/

1. Introduction

A three dimensional network of polymers made of natural or synthetic materials possessing high degree of flexibility due to large water content is called hydrogels. Under physiological conditions, they are able to retain a large amount of water or biological fluids and are characterized by a soft rubbery consistency similar to living tissues, making them an ideal substance for a variety of applications. Hydrogels with characteristic properties such as desired functionality, reversibility, sterilizability and biocompatibility meet both material and biological requirements to treat or replace tissues and organs, or the function of living tissues, as well as to interact with the biological system [1–3]. Hydrogels have been found in nature since life on Earth. Bacterial biofilms, which are hydrated extracellular matrix components, and plant structures are ubiquitous water swollen motifs in nature. Gelatine and agar were also known and used for various applications early in human history, but the modern history of hydrogels as a class of materials designed for biomedical applications can be accurately traced. In 1936, DuPont's scientists published a paper on the recently synthesized methacrylic polymers. In this paper, poly (2-hydroxyethyl methacrylate) (polyHEMA) was mentioned [4]. It was briefly described as a hard, brittle and glassy polymer, and was clearly not considered of importance. After that paper, poly HEMA was essentially forgotten until 1960. Wichterle and Lim [4] described the polymerization of HEMA and crosslinking agents in the presence of water and other solvents. Instead of brittle polymers, they obtained soft, water swollen, elastic and clear gel. This innovation led to the modern field of biomedical hydrogels, as we know them today. After that, the number of hydrogel formulations steadily grew over the years.

Problems like less solubility, high crystallinity, non-biodegradability; unfavourable mechanical and thermal properties, unreacted monomers and the use of toxic crosslinkers are the limitations of the hydrogel technology. Therefore, the development of these properties with new ideas would be possible with the combination of natural and synthetic polymers with pre-determined characteristics like biodegradation, solubility, crystallinity and biological activities. Hydrogels do not disintegrate during swelling, thanks to their crosslinked structure. Crosslinking may take place in two environments: in vitro, during the preparation of a hydrogel or in vivo (in-situ), after the application at a precise location of the human body. To initiate chemical crosslinking, it is necessary to introduce a low molecular weight crosslinking agent together with a polymer into the reaction mixture. In the absence of crosslinking points, the hydrophilic linear polymer chains dissolve in water due to the polymer chain and water thermodynamic compatibility. Nevertheless, in the presence of crosslinking points, solubility is counterbalanced by the retractive force of the elasticity of the crosslinking points in the network. When these forces become equal, then swelling reaches an equilibrium [5]. The hydrophilicity of the network is due to the presence of hydrophilic groups such $–NH_2$, –COOH, –OH, $–CONH_2$, –CONH–, and $–SO_3H$, capillary effect and osmotic pressure [6]. The chemical and physical crosslinking points maintain the 3D structure of hydrogels in the swollen state. In chemical crosslinking, the polymer chains are covalently bonded via a crosslinking agent, where in physical crosslinking the hydrogels possess physical domain junctions, hydrogen bonding, hydrophobic interaction, ionic complexation, which allows solvent casting, post process bulk modification, ease of fabrication, reshaping, biodegradation and non-toxicity showing better properties, which chemically crosslinked hydrogels lack [7].

Gibas and Janik [8] reported that the swelling of hydrogels is a complex process comprising of a number of steps. In the first step, the polar hydrophilic groups of the hydrogel matrix are hydrated by water, which appears in the form of primary bound water. In the second step, the water also interacts with the exposed hydrophobic groups, which appear in the form of secondary bound water. The primary

bound water and the secondary bound water both form the total bound water. In the third step, the osmotic driving force of the network towards infinite dilution is resisted by the physical or chemical crosslinks, so additional water is absorbed. The water absorbed into the equilibrium swelling is called the bulk water or the free water, which fills the spaces between the network or chains and the centre of the larger pores. The amount of water absorbed by a hydrogel depends on the temperature and the specific interaction between the water molecules and the polymer chains, which can be explained by the Flory–Huggins theory [9]. The solid portion of the hydrogel is a network of crosslinked polymer chains, a 3D network usually referred to as a mesh as shown in Fig. 1, with the spaces filled up with a fluid, normally water. The meshes hold the fluid and impart an elastic force that can be completed by the expansion and contraction of the hydrogel, and therefore are responsible for the solidity of the hydrogel. The ionic phase of hydrogels usually consists of ionisable groups bound onto the polymer chains and a number of mobile ions, including counter-ions and co-ions due to the presence of the electrolytic solvent, which surrounds the hydrogel.

Das [10] reported that interpenetrating polymers or networks (IPN) are generally formed of two or more polymer networks through the swelling of a first network in a solvent containing monomers, which then forms the second intermeshing network structure. The double networks of the IPN would either be hydrophobic or hydrophilic with the greater importance being holding the properties of the combination network [11]. The literature reports a number of classifications of hydrogels, and presents several views. Depending on the charges on the bound groups, hydrogels may be cationic, anionic or neutral. The types of crosslinking agent can be the criterion for classification; hydrogels can be physical or chemical. It is also possible to divide hydrogels into groups by their structure: amorphous, semi-crystalline, crystalline and hydrocolloid aggregates. Fig. 6 represents the classification of hydrogels based on their sources and properties, along with detailed classifications based on their response, i.e., physically, chemically and biochemically responsive hydrogels.

This review explores the applications of hydrogels in various fields including the biomedical, biotechnology, pharmaceutical and separation technology field. Due to the wonderful properties of the smart hydrogel, such as its reversible swelling/deswelling behaviour, high environmental sensitivity, high ionic conductivity, high permeability, surface properties, novel mechanical properties and sorption capacity, the hydrogel provides a platform for a range of applications including for microfluidic control, biomimetic, biosensor/bioactuator, bioseparation and artificial skin and muscles. The processing of hydrogels reported in this review is by a number of ways, classically by the one-step route of direct polymerization of the multifunctional monomer by crosslinking or multistep procedures, in which the first polymer is synthesized with specific functional groups and then reacted with a crosslinking agent as reported by Ahmed [12]. Different scientific approaches for the designing and processing of a specific hydrogel for a specific application are required to show maximum mechanical strength, chemical properties, stimuli response, density, biodegradation, and biological and environmental response. Solution polymerization and suspension polymerization are the most common techniques for the production of a variety of hydrogel networks with molecular-scale control over structure, such as crosslinking density, initiator, emulsifier and reaction conditions and tailored properties like chemical, physical and biological response to stimuli, mechanical strength, biodegradation and solubility.

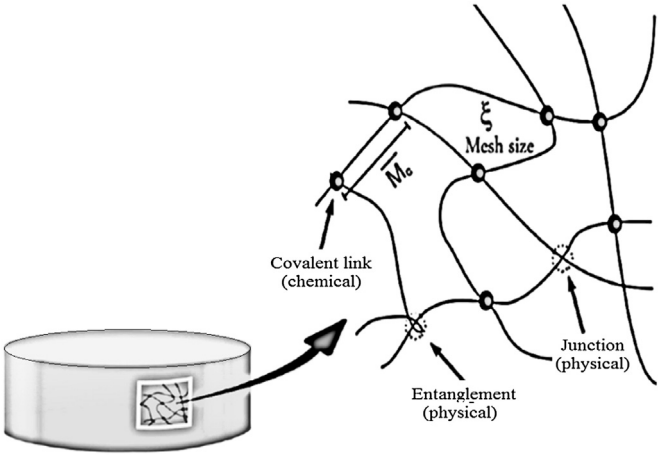

Fig. 1. Structural chemistry of a hydrogel [8].

About three decades ago, superabsorbent polymers (SAPs) were introduced and extended to industries where water holding ability was a major concern. In 1998, a different category of a water absorbent polymer system called super porous hydrogels (SPHs) was recognized to have better elastic properties, mechanical strength and water upholding ability [13]. This review gives a detailed literature for SAP and SPH evolution and differentiation, with a meaningful route for material engineers to process a hydrogel of their own interest. Presently, synthetic polymers have replaced natural polymer hydrogels because of their purity, high absorption capacity, well-defined structure, well-defined functionality, degradation and stability in varying ranges of pH, temperature, pressure and enzymes. Therefore, the combination of natural and synthetic polymers expands and their classifications also extends.

2. Classifications of hydrogels

The classification of hydrogels depends on their physical properties, nature of swelling, method of preparation, origin, ionic charges, sources, rate of biodegradation and observed nature of crosslinking [14]. It is clear from Fig. 2 that the classification details for each type are beyond the scope of this review, but some of the prominent hydrogels, which seriously attract scientists, are discussed.

In physical gels, the nature of the crosslinking process is physical. This is normally achieved via physical processes such as hydrophobic association, chain aggregation, crystallization, polymer chain complexion, and hydrogen bonding. On the other hand, a chemical process, i.e., chemical covalent crosslinking (simultaneously or post polymerization) is utilized to prepare a chemical hydrogel. Physical hydrogels are reversible due to the conformational changes where chemical hydrogels are permanent and irreversible because of configurationally changes.

Another category is the dual-network hydrogel, formed by the combination of physical and chemical crosslinked hydrogels due to an electrostatic interaction. It has recently been employed to overcome the disadvantages of solely using physical or chemical hydrogels with a high liquid uptake capacity over a wide range of pH and a higher sensitivity towards changes in the pH as compared to chemical hydrogels. Another dual-network consisting of graphene-polymer composites with superior mechanical properties and a self-healing ability was recently reported by Cong et al. [15] and Yalpani [16].

2.1. Crosslinking in hydrogels

Once crosslinks between the different polymer chains are introduced, the so obtained networks show visco-elastic and sometimes pure elastic behaviour. To review the crosslinking in hydrogels, the different scientific approaches are explained based on the physicals and chemicals in the proceeding section.

In the recent years, there has been increasing interest in physically crosslinked gels. The main reason is that the use of crosslinking agents to prepare such hydrogels is avoided. These agents cannot only affect the integrity of the substances to be entrapped (e.g., proteins, cells), but these agents are often toxic compounds which have to be

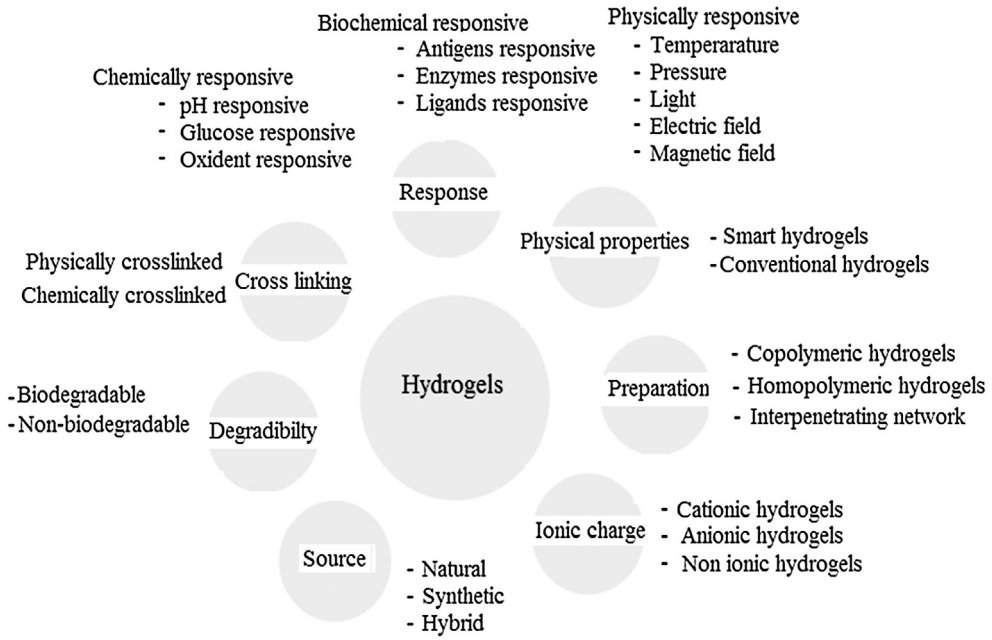

Fig. 2. Classification of hydrogels based on the different properties.

removed/extracted from the gels before they can be applied. To create physically crosslinked gels, different methods have been investigated.

2.1.1. Crosslinking by radical polymerization

One of the hydrogel characteristics is the swelling can be controlled by the amount of the crosslinker. Moreover, stimuli sensitive materials can be obtained by the addition of a crosslinker with predetermined properties. Other than radical polymerization of mixtures of vinyl-monomers, chemically crosslinked hydrogels can also be obtained by the radical polymerization of water-soluble polymers derivatized with polymerizable groups. Different water-soluble (synthetic, semi-synthetic and natural) polymers have been used for the design of hydrogels via this route.

2.1.2. Crosslinking by chemical reaction of complementary groups

Water-soluble polymers owe their solubility properties to the presence of functional groups (mainly OH, COOH, NH_2) which can be used for the formation of hydrogels. Covalent linkages between polymer chains can be established by the reaction of functional groups with complementary reactivity, such as an amine-carboxylic acid or an isocyanate–OH/NH_2 reaction, or by Schiff base formation.

Furthermore, crosslinking by condensation reactions, crosslinking by addition reactions, crosslinking by high energy irradiation and crosslinking using enzymes have been reported for the chemical hydrogels.

2.1.3. Crosslinking by ionic interactions

Alginate is a well-known example of a polymer that can be crosslinked by ionic interactions. Alginate is a polysaccharide with mannuronic and glucuronic acid residues and can be crosslinked by calcium ions [16]. Crosslinking can be carried out at room temperature and physiological pH. Therefore, alginate gels are frequently used as the matrix for the encapsulation of living cells [17] and for the release of proteins [110]. Interestingly, the gels can be destabilized by extraction of the Ca-ions from the gel by a chelating agent. The release of proteins from alginate microparticles, obtained by spraying a solution of sodium alginate into an aqueous solution of calcium chloride, can be modulated by coating the particles with cationic polymers, e.g., chitosan and polylysine [18]. A synthetic polymer that, like alginate, can also be crosslinked with Ca-ions is poly[di(carboxylatophenoxy)phosphazene] (PCPP). Gel microbeads are prepared by spraying an aqueous solution of PCPP in an aqueous solution of calcium chloride. The ionotropic hydrogels degrade under physiological conditions.

2.1.4. Crosslinking by crystallization

Poly(vinyl alcohol) (PVA) is a water-soluble polymer. When aqueous solutions of PVA are stored at room temperature they gradually form a gel, but with a low mechanical strength. Interestingly, once the aqueous solutions of this polymer undergo a freeze–thawing process, a strong and highly elastic gel is formed [19]. The properties of the gel depend on the PVA molecular weight, the PVA concentration in water, the temperature and time of freezing and the number of freezing cycles. Gel formation is ascribed to the formation of the PVA crystallites that act as physical crosslinking sites in the network. Gels prepared using optimized conditions are stable for 6 months at 37 °C [20].

Physically crosslinked hydrogels are generally obtained from multiblock copolymers or graft copolymers. The latter can be composed of a water-soluble polymer backbone, for example a polysaccharide, to which hydrophobic units are attached, or hydrophobic chains containing water-soluble grafts. Other reported methods used for crosslinking include hydrogen bonding [15], suspension polymerization [21], irradiation chemical reaction of identical groups [22] and protein crosslinking [23], but involve the use of a crosslinking agent, which is often toxic and raise concerns regarding the gel reliability. For these reasons, physically crosslinked hydrogels, which can be prepared by several crosslinking methods such as ionic interaction crystallization, hydrogen bonding, protein interaction and hydrophobic interaction [24], now exist.

Due to their water-absorbing capacity, hydrogels are not only the subject of investigation by researchers interested in the fundamental aspects of swollen polymeric networks, but have also found widespread application in different technological areas. These include material for contact lenses and protein separation, matrices for cell-encapsulation, devices for the controlled release of drugs and proteins, nutrient carrier for soil, cosmetics and enhanced oil recovery. The reader is referred to a variety of excellent books and review papers that describe the fundamental aspects and application areas of hydrogels.

Based on the nature of the side groups, these hydrogels can be classified as neutral or ionic, where in neutral hydrogels the dynamic force for swelling is due to the water–polymer thermodynamic mixing,

which contributes to the overall free energy, along with elastic polymer with their effects for biomedical applications [20]. The physical properties of the network include amorphous, semi-crystalline, hydrogen bonded structures, super-molecular structures and hydrocolloid aggregates [25].

2.2. Interpenetrating network hydrogels

Based on the methods of preparation, hydrogels may be classified as (1) homo-polymers, (2) copolymers, (3) semi-interpenetrating networks and (4) interpenetrating networks. Homo-polymer hydrogels are crosslinked networks of one type of hydrophilic monomer unit, whereas copolymer hydrogels are produced by the crosslinking of two co-monomer units, at least one of which must be hydrophilic to render them swellable. Finally, interpenetrating polymeric hydrogels are produced by preparing a first network that is then swollen in a monomer. The latter reacts to form a second intermeshing network structure.

2.2.1. Homo-polymeric hydrogel

Homo-polymers refer to polymer networks derived from single species of monomer. It is the basic structural unit, comprising of any polymer network [26]. Homo-polymers may have a crosslinked skeletal structure depending on the nature of the monomer and polymerization technique. Polyethyleneglycol (PEG) based hydrogels are responsive towards external stimuli and hence, these smart hydrogels are widely used in drug delivery systems. Chemically crosslinked PEG hydrogels are used as scaffolds for protein recombination and functional tissue production. It is a suitable biomaterial for the efficient and controlled release of drugs, proteins, biomolecules and growth factors [27].

2.2.2. Co-polymeric hydrogel

Co-polymeric hydrogels are composed of two types of monomer in which at least one is hydrophilic in nature. Gong et al. [28] synthesized the biodegradable triblock poly(ethylene glycol)-poly(ε-caprolactone)-poly(ethylene glycol) (PECE) co-polymeric hydrogel for the development of drug delivery systems. The mechanism involved here is the ring-opening copolymerization of ε-caprolactone. In the triblock synthesis, mPEG was used as the initiator, stannous octoate as the catalyst and hexamethylene diisocyanate as the coupling agent. This co-polymeric block is capable of forming a hydrogel when it is applied in-situ.

2.2.3. Semi-inter penetrating network (semi-IPN)

If one polymer is linear and penetrates another crosslinked network without any other chemical bonds between them, it is called a semi-inter penetrating network [29]. Semi-IPNs can more effectively preserve rapid kinetic response rates to pH or temperature due to the absence of a restricting interpenetrating elastic network, while still providing benefits like modified pore size and slow drug release. One example to justify the situation is the entrapment of linear cationic polyallylammonium chloride in acrylamide/acrylic acid copolymer hydrogels, which impart both higher mechanical strength and a fully reversible pH switching of theophylline release. This pH sensitive semi-IPN was synthesized by template copolymerization in the presence of *N*, *N*′-methylene bisacrylamide as a crosslinking agent [21]. The network contained both covalent and ionic bonds. The covalent bonds retained the three-dimensional structure of the hydrogel and the ionic bonds imparted higher mechanical strength and pH responsive reversibility to the hydrogel.

2.2.4. Inter penetrating network (IPN)

IPNs are conventionally defined as the intimate combination of two polymers, at least one of which is synthesized or crosslinked in the immediate presence of the other [30]. This is typically done by immersing a pre-polymerized hydrogel into a solution of monomers and a polymerization initiator. The IPN method can overcome the thermodynamic incompatibility that occurs due to the permanent interlocking of network segments and a limited phase separation can be obtained. The interlocked structure of the crosslinked IPN components are believed to ensure the stability of the bulk and surface morphology [31]. The main advantages of IPNs are that relatively dense hydrogel matrices can be produced which feature stiffer and tougher mechanical properties, controllable physical properties and a more efficient drug loading compared to conventional hydrogels. Drug loading is often performed in conjunction with the polymerization of the interpenetrating hydrogel phase [31]. The IPN pore sizes and surface chemistries can also be controlled to tune the drug release kinetics, and the interaction between the hydrogel and the surrounding tissues along with its mechanical properties [32].

2.3. Stimuli responsive hydrogels

Stimuli responsive hydrogels respond to environmental stimuli and experience unexpected changes in their growth actions, network structure, mechanical strength and permeability, hence called environmentally sensitive, smart hydrogels [5,33]. Physical stimuli include light, pressure, temperature, electric fields, magnetic fields, mechanical stress and the intensity of various energy sources, which change molecular interactions at critical onset points. Chemical stimuli include pH, ionic factors and chemical agents, which change the interactions between polymer chains and solvents and between polymer chains at the molecular level.

Another class, which is called dual responsive hydrogels, results from a combination of two stimuli responsive mechanisms in one hydrogel system. Polyacrylic acid-co-polyvinyl sulfonic acid is an example of a dual responsive polymer system [34]. A biochemical stimulus involves the responses to ligand, enzyme, antigen, and other biochemical agents [5,33]. So, stimuli responsive hydrogels are attractive biomaterials for pharmaceutical, biomedical, and biotechnology applications [35].

2.4. pH responsive hydrogels

Patel and Mequanint [36] reported polymeric hydrogels with ionic pendant groups that can accept or donate protons in response to an environmental pH change. In a pH responsive hydrogel at a specific pH, the degree of ionization known as pK_a or pK_b, is dramatically changed. This rapid change in the net charge of the ionized pendant group causes a sudden volume transition by generating electrostatic repulsive forces between the ionized groups, which creates a large osmotic swelling force. There are two types of pH responsive hydrogels: anionic and cationic hydrogels. Anionic hydrogels have pendent groups such as carboxylic or sulfonic acid, where deprotonation occurs when the environmental pH is above the pK_a leading to the ionization of the pendent groups, which in turn, increases the swelling of the hydrogel [37–39]. On the other hand, cationic hydrogels contain pendent groups such as amine groups, where ionization takes place below the pK_b, which increases swelling due to the increased electrostatic repulsions [24,40].

2.4.1. Properties of pH responsive hydrogels

Gupta et al. [24] suggested that the degree of swelling of ionic hydrogels is controlled by major factors. The first factor is the properties of the polymers such as concentration, crosslink density, ionic charge, pK_a or pK_b of the ionisable groups, hydrophilicity or hydrophobicity and the degree of ionization. The second factor includes the properties of the swelling medium like pH, ionic strength, counterion and the valency of the polyvinyl sulfonic acid (PVSA) [41,42]. Bossard et al. [43] reported the ability of polydiethylaminoethyl methacrylate (PDEAEMA) and their copolymer to ionize in response to pH as shown in Fig. 3.

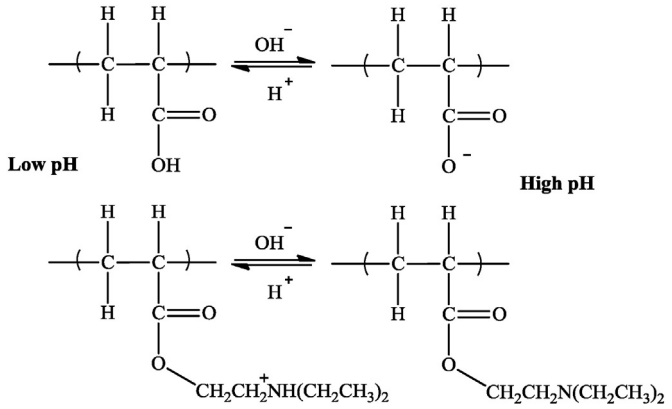

Fig. 3. pH dependent ionization of polyelectrolyte.

Dolatabadi et al. [44] reported alginate-N, O-carboxymethyl chitosan (NOCC) gel beads coated with chitosan for colon specific drug delivery. Their studies concluded that the degree of swelling at pH 7.4 was considerably higher than at pH 1.2, which indicate the pH sensitivity of these hydrogels. Swelling properties were observed to decrease due to the presence of NOCC and by chitosan coating due to the H-bonding and ionic interaction of the functional groups of polymer chains.

2.4.2. Limitations and improvements

Sadeghi and Hosseinzadeh [45] reported a starch-poly (sodium acrylate-*co*-acrylamide) superabsorbent hydrogel with pH responses and also studied the release profile of ibuprofen in simulated gastric and intestinal pH conditions. The swelling rate with various particle sizes was investigated and it was observed that the release was much quicker at pH 7.4 compared to pH 1.2. The non-biodegradability is not a problem in certain applications, such as in oral drug delivery, but it is a serious limitation in other applications like drug delivery and in the agent's implantable biosensors. Therefore, attention has been given to the development of pH-sensitive biodegradable and biocompatible hydrogels based on polysaccharides, polypeptides and proteins.

2.5. Temperature responsive hydrogels

2.5.1. Properties of temperature responsive hydrogels

Temperature sensitive hydrogels are defined by their ability to swell and shrink when the temperature changes in the surrounding fluid, which means the swelling and deswelling behaviour mostly depend on the surrounding temperature [46]. Temperature responsive hydrogels can be classified as positive or negative temperature responsive systems [47].

2.5.1.1. Positive temperature hydrogels. Positive temperature hydrogels are known by the upper critical solution temperature (UCST) [48]. This means that when the temperature is below the UCST, the hydrogels contract and release solvents or fluids from the matrix (de-hydration). At temperatures higher than the UCST, swelling takes place. In view of the above, it can be concluded that these types of hydrogels are retrogressive at negative temperatures. Positive temperature hydrogels shrink at low temperatures because of the formation of a complex structure by the hydrogen bonds. The structure dissociates at a high temperature due to the breaking of the hydrogen bonds, and the gel will swell to the maximum possible extent rapidly above the UCST. There are a lot of polymers and copolymers that are positively temperature dependent, such as poly (AAm-co-BMA), and the random copolymer gel, poly (AA-co-AAm-co-BMA) [49].

Kashyap et al. [35] studied physically crosslinked thermo sensitive hydrogels and concluded that they may undergo sol–gel phase transitions instead of a volume change at a critical solution temperature. The most-studied temperature responsive hydrogels are chitosan-based copolymers i.e., methylcellulose, hydroxypropyl methylcellulose and N-isopropylacrylamide (NIPAAm) [3,50,51]. Poly(*N*-isopropylacrylamide) (PNIPAAm) is the most popular temperature responsive polymer that shows a sharp phase transition in water at 34.3 °C, which is close to physiological temperature, but (PNIPAAm) LCST can be controlled by copolymerization with other monomers. The LCST increases with the addition of hydrophilic monomers, and it decreases with the incorporation of hydrophobic monomers. On the other hand, the grafting of hydrophilic or hydrophobic monomers does not show any considerable change in the LCST.

2.5.1.2. Negative temperature-PHGs. This kind of hydrogel has a critical parameter called low critical solution temperature (LCST), which means that the hydrogels will shrink when the temperature increases above the LCST and will show a swelling behaviour when lower than the LCST. The LCST is the most important parameter for negative temperature-sensitive hydrogels and can be changed in different ways, such as by mixing a small amount of ionic copolymer in the gels or by changing the solvent composition. In general, the LCST of a polymer with more hydrophobic constituent shifts to lower temperatures [52]. By changing the ratio of hydrophobic to hydrophilic content of the structure of hydrogels, the LCST will be changed. Such hydrogels have two parts; the first is the hydrophilic part –CONH–, and the second is hydrophobic part –R– [53]. At temperatures lower than the LCST, water or fluid interact with the hydrophilic part by forming hydrogen bonds. Because of these hydrogen bonds, the dissolution and swelling will improve. As the temperature increases to greater than the LCST, the hydrophobic interaction with the hydrophobic part will be stronger, while at same time, the hydrogen bonds will become weaker. Therefore shrinking of sample will occur due to the inter-polymer chain association [54], and the absorbed fluid will go out through a de-swelling process. An example is the PVP/PNIPAAM based negatively thermosensitive drug release hydrogel.

A number of hydrogels formed by IPNs show positive thermosensitivity i.e., they shrink at low temperatures and swell at high temperatures. Poly(acrylic acid) and polyacrylamide (PAAm) or P(AAm-*co*-BMA) perform as positively thermosensitive hydrogels, as reported by Katono et al. [55]. It was observed that increasing the BMA content shifted the transition temperature to higher temperature. The swelling of the hydrogels was reversible, corresponding to the stepwise temperature changes. This resulted in reversible changes in the release rate of a model drug, ketoprofen, from a monolithic device. Geever et al. [56] studied PVP/PNIPAAM copolymeric hydrogels as negative temperature responsive hydrogels. He concluded that the drug was released at a slower rate above the lower critical solution temperature (LCST). The decrease in transition temperature was observed with the incorporation of crosslinking agents and it was also observed that maximum swelling occurred at temperatures above the transition temperature for both types of copolymer. Furthermore, the drug was released at a constant rate because the gel did not swell or shrink due to the balancing of the hydrophilic–hydrophobic interactions.

2.5.1.3. Thermo-reversible hydrogels. These kinds of hydrogel have the same structure and content as that of negative and positive temperature hydrogels. The difference with the previous two types of thermosensitive hydrogels is in their bond types. The polymer chains in this class are not covalently crosslinked, and the gel will undergo a sol–gel phase transition instead of a swelling-shrinking transition.

Chemically crosslinked thermo-sensitive hydrogels undergo volume changes rather than sol–gel transitions. Certain molecular interactions, such as hydrophobic associations and hydrogen bonds, play a vital role in the abrupt volume change of these hydrogels at the Critical Solution Temperature (CST). In the swollen state, water molecules form hydrogen bonds with polar groups of polymer backbone within

the hydrogels and organize around hydrophobic groups as iceberg water. At the CST, hydrogen bonding between the polymer and water becomes unfavourable compared to polymer–polymer and water–water interactions, which force the quick dehydration of the system and the release of water out of the hydrogel with a large gain in entropy, resulting in shrinkage of the polymeric structure [47]. PEO–PPO–PEO is an example of thermoreversible-based hydrogel. For parental applications of thermoreversible hydrogels, it is very important that they are biodegradable. So, to introduce biodegradability, the PPO segment of the PEO–PPO–PEO is usually replaced by poly(L-lactic acid). In effect, the proper architecture and proper molecular weight combination results in a hydrogel with varying LCST values at room and body temperatures.

Thermally reversible hydrogels represent the most important class of hydrogels, the aqueous solutions, which undergo sol to gel transitions in response to certain stimuli. Polymers with hydrophobic domains can be crosslinked in an aqueous medium by reverse thermal gelation, where the hydrophobic segment is coupled to the hydrophilic segment by grafting or copolymerization and such amphiphiles are soluble in water at low temperatures. If the temperature increases, the entropy of the solvent increases and the hydrophobic domain aggregates to minimize their surface area. Therefore, the temperature at which gelation occurs is dependent on the polymer concentration, hydrophilic and hydrophobic blocks and the chemical nature of the polymers. The reversible sol–gel transition is clear in Fig. 4.

Li et al. [57] reported Pluronics and Tetronics, the most commonly used thermo-reversible hydrogels approved by the FDA and EPA for applications in food additives, pharmaceutical ingredients and agricultural products.

2.5.2. Limitations and improvements

The limitations of the thermo-sensitive hydrogel based on PNIPAAM and its derivatives are the non-biodegradability and non-biocompatibility of their monomers and crosslinkers, which may lead to toxic, carcinogenic and teratogenic effects. The observation that acrylamide-based polymers activate platelets upon contact with blood, together with the unclear metabolism of PNIPAAM, requires detailed toxicity studies before applications. In addition, the development and improvement in the production of new biodegradable and biocompatible thermo-sensitive hydrogels are necessary to exploit the useful properties of these hydrogels.

2.6. Glucose responsive hydrogels

2.6.1. Properties of glucose responsive hydrogels

For diabetes treatment, in order for the glucose-sensing carrier to trigger the release of insulin, suitable insulin delivery hydrogel systems should be developed. Glucose sensitive hydrogels are attractive insulin carriers and glucose oxidase mixtures. Podual [58] and Brahim et al. [59] suggested a class of material called "bio-smart", in which engineered molecular recognition is coupled with actuation, consisting of HEMA and PMA. The local pH of the system is reduced when glucose is converted to gluconic acid by glucose oxidase in the presence of oxygen, which increases the swelling of cationic hydrogels and releases insulin. To reduce its fast diffusion out of the system and improve the controlled loading of insulin, glucose oxidase has been covalently tethered onto the hydrogel system.

2.6.1.1. Glucose oxidase based hydrogels. Other mechanisms including the use of concanavalin-A as a crosslinker, and phenylboronic acid or glucose dehydrogenase as a biosensor have been also investigated to formulate glucose responsive hydrogels, as reported by Misra et al. [60]. Glucose oxidase is the most widely used enzyme in glucose-sensing as it oxidizes glucose into gluconic acid, thus changing the pH of the system, which enables the use of a variety of pH sensitive hydrogels for controlled insulin delivery. Lowering the pH in PDEAEM-based hydrogels results in swelling due to ionization and releases insulin and other drugs. A glucose sensitive hydraulic flow controller can be designed using a porous membrane filter grafted with polyanions like (methacrylic acid-co-butyl methacrylate) and immobilized glucose oxidase. Therefore, at normal pH, the chain expands. But, as the glucose is being converted into gluconic acid by glucose oxidase, the pH decreases and the chains collapse due to the protonation of the carboxyl groups.

2.6.1.2. Concanavalin A based hydrogels. Concanavalin A (Con-A) is a glucose binding protein obtained from the jack bean plant *Canavalia ensiformis* [57]. The free glucose molecules compete with glucose-insulin conjugates bound to Con A. Thus, glycosylated insulin is desorbed in the presence of the free glucose. Glucose–insulin conjugates are released into the surrounding tissues, where they show their bioactivity depending on the different glucose levels. As the external glucose molecules diffuse into the hydrogel, the free glucose molecules compete with the polymer-attached glucose and exchange with them. Therefore, the concentrations of Con A and glucose containing polymers can be adjusted to make hydrogels that respond to a specific free-glucose concentration. Glucose sensitive hydrogels can also be prepared without the use of Con A. Polymers with phenyl boronic groups, like poly(3-(acrylamide) phenyl boronic acid) and its copolymers.

2.6.1.3. PVA based hydrogels. Polyvinyl alcohol (PVA)-based hydrogels form a gel through the complex formation between the pendant phenylborate and hydroxyl groups, while compete with polyol polymers for the borate crosslinking. Since glucose is monofunctional (one binding site), it cannot act as a crosslinking as polyol functions. Thus, the glucose concentration increases as the crosslinking decreases, which results in the swelling of the hydrogel and favours with the release of insulin as shown in Fig. 5.

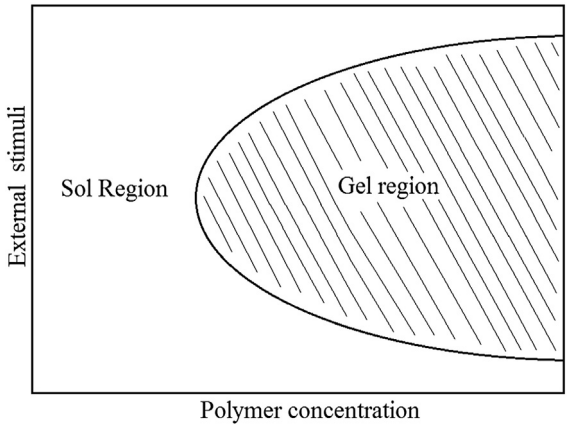

Fig. 4. Sol to gel transition in stimuli responsive hydrogels.

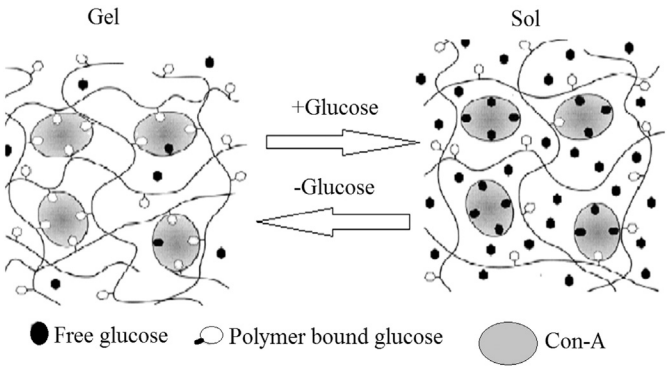

Fig. 5. Sol–gel transition of a glucose sensitive hydrogel [14].

2.6.2. Limitations and improvements of temperature responsive hydrogels

Glucose sensitive hydrogels are known to be promising, but they show very slow response and do not go back to their original condition fast enough after responding to glucose concentrations. An additional constraint in glucose responsive hydrogels is that they should be biocompatible, e.g., the Con-A used in such delivery systems are thought to induce undesirable immune responses. Hence, many improvements are needed for them to become clinically useful, in which the hydrogels must respond to every change in the glucose concentration at all times with good reproducibility, quickly and for a longer period.

2.7. Protein-based hydrogels

Such hydrogels are specifically designed with pre-defined sequences, compositions, stereochemistry and molecular weights using recombinant DNA technology for drug delivery and tissue engineering applications. Coiled-coil is an attractive approach for protein-based hydrogels. In protein-based polymeric hydrogels, the hydrophobic amino acid residues of the coiled-coil proteins are used as physical crosslinkers as shown in Fig. 6. Further, in physically crosslinked protein-based hydrogels, the tri-block copolymers with coiled-coil domains at the end and water-soluble polypeptide domains at the centre have been investigated by Kopeček and Yang [61]. Consequently, temperature and pH-responsiveness may be achieved by manipulating the amino acid sequences of the coiled-coil domains and cell interactions can be improved by knowing the hydrophilic polypeptide sequence. Moreover, in order to prepare the 3D structure of the hydrogels, water soluble linear synthetic polymer coiled-coil proteins are used as crosslinkers [62].

Ulijin et al. [63] studied the utility of fluorescence correlation spectroscopy (FCS) to measure albumin diffusion rates and concentration profiles above the cell surface and overlying the intercellular junctions of lung capillary endothelial cells. The results suggest a structure interacting with albumin from 1 to 2 μm above the cell membrane, which is capable of reducing the albumin diffusion by 30% while simultaneously increasing the albumin concentration five-fold. Fig. 7 represents the first use of FCS to probe extracellular structures and to understand the structure–function relationship of the lung's microvascular endothelial glycocalyx. The author suggested that hydrogels used for protein delivery exhibit characteristic properties as they create a steric hindrance to the diffusion of proteins. Furthermore, these chains are also 'sticky' to the proteins and the weak association further slows the protein diffusion.

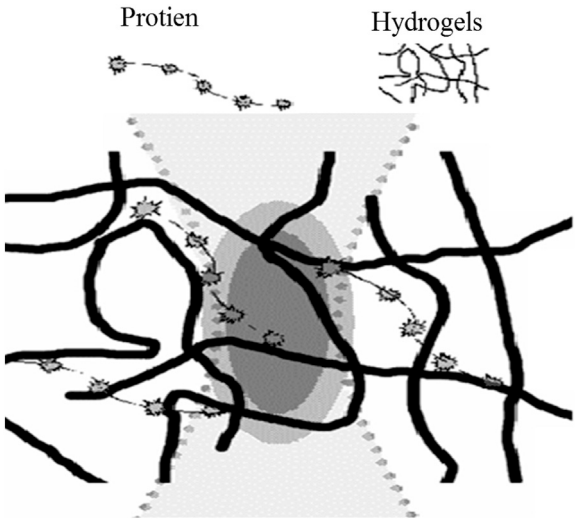

Fig. 7. Observation volume of FC superimposed on hydrogen with diffusing [63].

2.8. Antigen-responsive hydrogels

Antigen-responsive hydrogels are designed by grafting antigens on hydrophilic polymeric backbones to deliver biomolecules at a specific targeted site [64]. These hydrogels can be mixed with antibody-grafted crosslinked hydrophilic polymeric backbones. In the absence of a free antigen, the structure of the hydrogel shrinks due to intra-chain antigen-antibody binding in the polymer network. Formulating an antigen-sensing device make them useful biomaterials for biomolecules, protein or drug delivery at desired sites, where the remarkable feature is specific molecular recognition of antigen-sensitive hydrogels. Miyata et al. [65] reported an antigen responding hydrogel, which can be prepared by grafting antigen and the corresponding antibody to the polymer network, so that the binding between the two introduces crosslinks into the network [64,65]. According to the author, competitive binding of the free antigen triggers a change in the hydrogel volume, owing to the breaking of these non-covalent crosslinks as shown in Fig. 8. They also reported that hydrogels display shape memory behaviour and pulsatile permeation of protein through the network by a stepwise change in the antigen concentration.

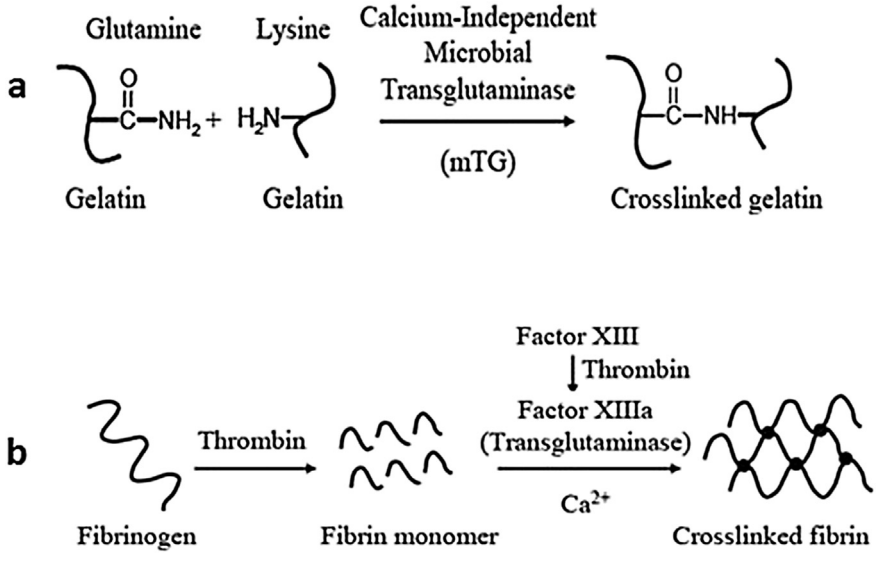

Fig. 6. Protein based hydrogels [61].

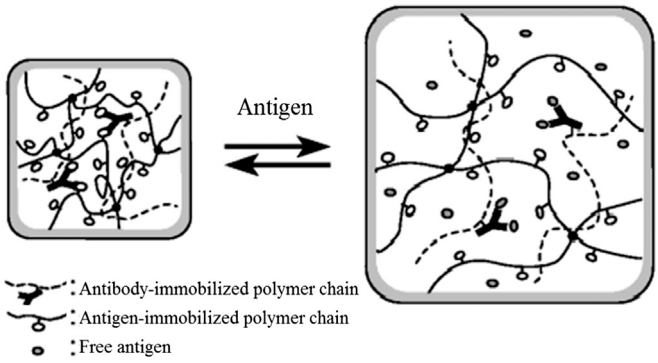

Fig. 8. Swelling of an antigen-antibody semi IPN hydrogel in response to a free antigen [65].

3. Applications of hydrogels

Hydrogels are momentous collection of resources with incredible purposes in engineering, biology and pharmaceutical sciences. Polyelectrolyte hydrogels are especially useful as they either carry or develop charges on the chain, and bind with opposite-charged species to form complexes, which highlight their numerous applications in drug delivery, protein, peptide, pesticides nutrient, hormone, agriculture, horticulture, biotechnology, cell construction, pharmaceutical and biomedical applications. Among the synthetic carriers, cationic polymers receive greater attention, because they are able to reduce large structures into smaller ones, and cover negative DNA charges, which are required for transfecting most types of cells, gene, antisense therapies and bile acid sequestrates, and for developing viral and non-viral vectors for DNA and oligonucleotide delivery. Hydrogels exhibit considerable volume changes in response to small changes in their surroundings, such as changes in the electric field, magnetic field, solvent, pH, ionic strength and temperature.

3.1. Biomedical applications

Hydrogels copy the behaviour of human organs in response to changes in the environmental conditions such as pH, temperature, enzymes and electric field, which find applications in medical implants, prosthetic muscles or organs, robotic grippers, diagnostic devices to artificial muscles, stabilization of bone implants, intimal thickening in animals and decreasing thrombosis [66–69]. Hydrogels used in urinary catheters can prevent bacterial colonization on the surface, and provide a smooth and slippery surface to improve its biocompatibility. One of the advanced applications of hydrogels reported by Park et al. [70], is their ability to convert electrochemical stimuli into mechanical work (contraction), i.e., reversible contraction and relaxation under physicochemical stimuli for the development of artificial muscles, which function like the human muscle and tissue but with an electrically driven muscle like actuators.

3.1.1. PEG–PLGA based hydrogels

Jeong and Gutowska [71] reported PEG–PLGA graft copolymeric hydrogels based on the concept of molecular recognition for cancer treatment and cancer imaging, using light-sensitive polymers with stimuli-sensitive properties for potential biomedical applications. They suggested that a good delivery system should be able to cross the cell membranes, target specific tissues, facilitate nuclear uptake, offer conflict to enzymatic aggregation and degradation, and supply genetic material, with no toxicity or immune response. The specified applications under controlled conditions make the hydrogel a very prominent subject for a variety of research areas, which confirms the smart nature of these hydrogels, to be applied mainly under the given headings.

3.1.2. PPO–PEO based hydrogels

Corkhill et al. [72] reported PPO–PEO hydrogels and concluded that they form a clear gel at body temperature, fill the spaces in a wound and isolate the area from bacterial infection so they are used as wound dressing materials with high flexibility, durability, and permeability to water vapour and metabolites, which completely cover the wound. Hydrogels as contact lenses and intraocular lenses are other applications of hydrogels. Hydrogels used in soft intraocular lenses have an advantage over the rigid types with high oxygen permeability, although they have problems of protein deposits and lens spoliation. Bontempo et al. [73] investigated the mechanism of protein lipid interactions responsible for biofilm formation on the surface of permeable contact lenses made up of siloxanyl alkyl acrylate and fluorosiloxanyl alkyl acrylate poly poly(SAA–FSAA) and showed that the presence of lipids in artificial tear solutions enhances the deposition of proteins on the lenses. It was demonstrated that the hydrophobic sites of the lipid molecules are attracted to the lens matrix, while the more hydrophilic sites are repelled by the matrix and thus exposed to the aqueous surroundings. Thus, lipids bound to the lens matrices reduce the hydrophobicity of the lens surface, allowing proteins to bind and these bound deposited proteins thus change the subsequent binding of both proteins and lipids.

3.1.3. Methylcellulose-PEG hydrogels

Darsow et al. [74] reported methylcellulose-PEG based hydrogels, which can be applied to prevent skin irritation. He suggested that the methylcellulose-PEG hydrogel could be used to deliver allergens in skin testing, as less skin irritations and skin abrasions were observed when test allergens were delivered in the hydrogel vehicle.

3.2. Biotechnology application

Hydrogels have been used as immediate matrix membranes in sensors with desired hardness, elasticity, selective diffusion of analyte and refractive indices. Smart hydrogels have been used to concentrate dilute aqueous solutions of macromolecular solutes, including proteins and enzymes, without disturbing the activity of the enzyme by adjusting the temperature or pH of the environment depending on the size and net charge [75,76]. Smart hydrogels in solutions, by reversible swelling and shrinking in response to a small change in the environmental situation, are also functional in purification devices [77]. Immobilizing the adsorbents into hydrogels such as agarose and calcium alginate gel is effective to prevent fouling of the adsorbent by colloidal contaminants. By changing the swelling behaviour, hydrogels have been reported to control the reactions of substrates with immobilized enzymes [70,78]. It was observed that steroid conversion was higher in more hydrophobic gels due to the high partitioning of water-insoluble steroids [70].

3.2.1. PEtOz–CHMC based hydrogels

Yuan et al. [79] studied poly(2-oxazoline)–cholesteryl methyl carbonate (PEtOz–CHMC) and showed that PEtOz is a promising biomaterial for the modification of liposomes in drug delivery. Confocal laser scanning microscope observations revealed that this hydrogel responded to low endosomal pH and directly released the fluorescent tracer into the cytoplasm. It was also concluded that Doxorubicin hydrochloride-loaded PEtOz hydrogels exhibited stronger anti-tumour activity in a medium at pH 6.4 than in a medium at pH 7.4.

3.2.2. Imprinted hydrogels

Whitcombe et al. [80] studied smart imprinted hydrogels and concluded that as the analyte replaces the pendant analyte groups in the protein, the network loses effective crosslinks, opens the network mesh size and regulates release. Consequently, as the analyte decreases in concentration, the protein binds again with the pendant analyte groups, closing the network structure. Thus, hydrogels will release

competitive binding responses to free analytes in the solution. As seen clearly in Fig. 9, the binding of molecules to active sites can indeed change the hydrophilicity or hydrophobicity, and thus, the swelling of a hydrogel. Fig. 9 represents the analyte (A) binding the covalently attached enzyme (E). So, for cationic hydrogels, which are weak and basic, the results are ionization, swelling and the release of drugs, peptides or proteins (filled circles). At specific concentrations, (B) represents analytes. When competing with the protein, the analyte binds with the protein, and effective crosslinks are reversibly lost and release occurs. (C) represents analyte-induced swelling. (D) represents analyte binding groups randomly introduced into the network during polymerization to show the analyte attaching to the drug, peptide or protein as the analyte competes for binding sites. The release occurs as shown in Fig. 9.

3.3. Pharmaceutical applications

3.3.1. PVA based hydrogels

Its common applications include insulin, stomach, liver, colon, intestinal, brain, blood, nervous system and tumour-targeted delivery. Controlled drug delivery is an important factor for the application of hydrogels in the pharmaceutical industry. Kim and Lee [81] studied composite PVA beads for controlled drug delivery with a double layered structure with the conclusion that release time can be further extended by increasing the PVA and its degree of crosslinking.

3.3.2. PEG–PCL based hydrogels

Diacrylates of PEG and PCL for controlled drug delivery and tissue regeneration are hydrogels that exhibited negative thermosensitive swelling behaviour due to hydrophilic and hydrophobic block copolymers. The in vitro degradation tests showed that degradation occurred over a 3 to 8 month period. Therefore, due to their biodegradability, biocompatibility, elasticity and functionality, these hydrogels are suitable for pharmaceutical applications.

3.3.3. PHEMA-co-DMAEMA based hydrogels

Zero-order drug kinetics is vital for most drugs; hence, many drugs need a release drift to be delivered which the hydrogel can fulfil. Hydrogels, in relation to glucose intensity, is capable of releasing additional insulin. Such systems include pH-sensitive polymers such as (PDEAEMA) and glucose oxidase, which convert glucose into gluconic acid and control insulin release [82–84]. Traitel et al. [82] studied insulin release systems in simulated in vivo conditions consisting of poly(2-hydroxyethyl methacrylate-co-*N*,*N*-dimethylaminoethyl methacrylate), also called poly(HEMA-co-DMAEMA), with entrapped glucose oxidase, catalase and insulin as shown in Fig. 10. It was concluded that when these hydrogels are exposed to physiological fluids, the glucose diffuses into the hydrogels, whereby the glucose oxidase is a catalyst for the glucose conversion to gluconic acid, which causes the swelling of the pH sensitive hydrogels and releases the insulin. It was also concluded that hydrogels without crosslinking were found to be stable in water and their swelling and sensitivity towards glucose was higher than chemically crosslinked hydrogels. The chemistry of oxidation and catalysis is represented in the form of an equation shown as:

$$\mathrm{Glucose} + O_2 + H_2O \xrightarrow{\mathrm{GluOx}} \mathrm{Gluconic\,Acid} + H_2O_2$$
$$H_2O_2 \xrightarrow{\mathrm{Catalase}} {}^1/_2O_2 + H_2.$$

The above represents a summary of the swelling and release mechanism as shown in Fig. 10.

3.3.4. PNIPAAM–PEGDA based hydrogels

Temperature-responsive hydrogels are typically made of polyacrylamide derivatives and are efficient in the pulsatile release of drugs where hydrophobic interactions are required for shrinking at well-known temperatures. Thus, the release of drug delivery can be turned on and off at will. Ramanan et al. [85] investigated the development of a temperature sensitive composite hydrogel for pharmaceutical applications based on PNIPAAM–PEGDA. Additionally, both micro- and nano-particles had excellent loading efficiency (>80% of incubated

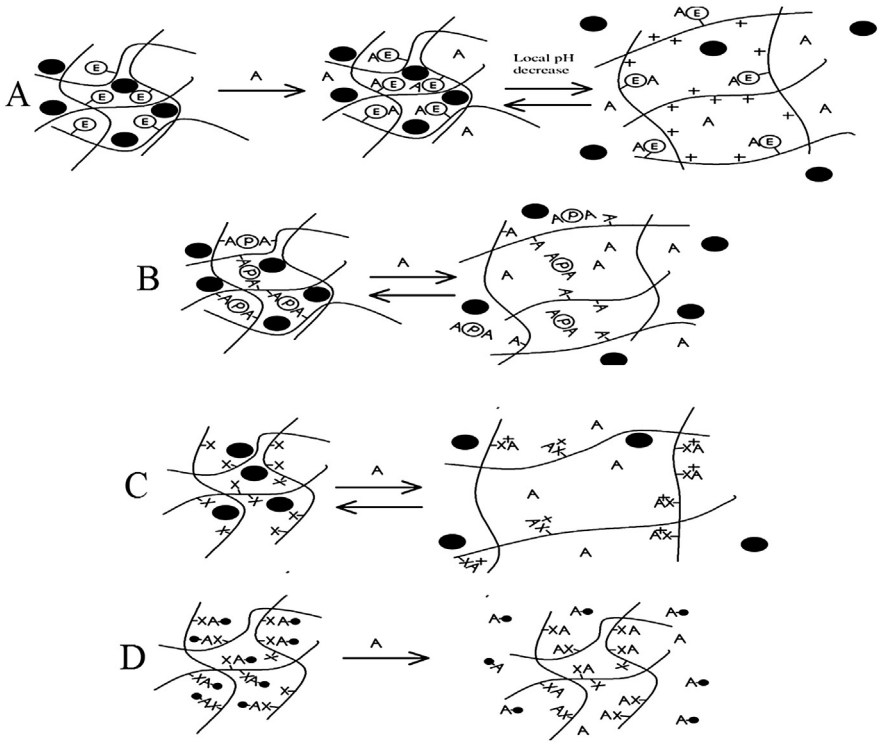

Fig. 9. Smart analyte-sensitive hydrogels [80].

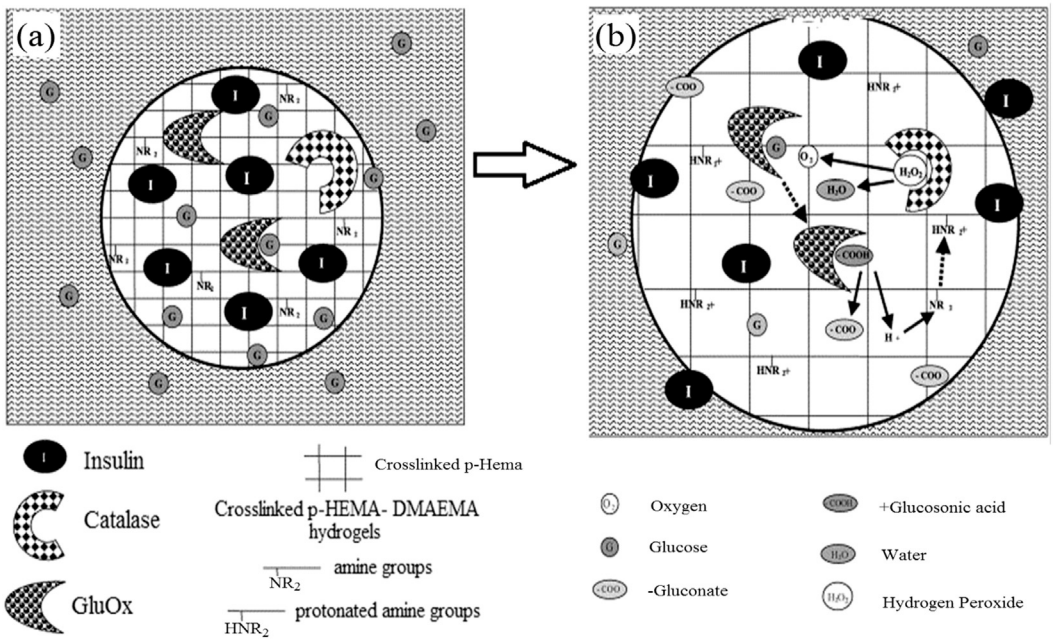

Fig. 10. Schematic presentation of unswollen/swollen hydrogel on p(HEMA–DMAEMA) [82].

blood serum albumin BSA). The results showed temperature sensitivity with an advantage of in situ polymerization to localize at a specific region [65,86].

3.4. Separation technology

Water pollution is a massive environmental problem as a variety of dyes used in the plastic, paper, cosmetic and textile industries are discharged in large amounts, and are non-biodegradable, toxic and carcinogenic. Conventional approaches like coagulation, chemical precipitation, solvent extraction, membrane filtration, oxidation and biological treatment are engaged for the removal of these dyes from industrial wastewaters, which are not always efficient. Hence, the concept of adsorption is considered an economical and effective method to remove these dyes, with properties like flexibility in the selection of an adequate sorbent, and in the operation and fabrication of effluents suitable to be reused [87,88]. So, attempts to prepare membranes with fast adsorption/desorption rates, easy separation, regeneration and high adsorption capacities have strongly increased recently [89,90]. Similarly, heavy metal ions, which are highly toxic, non-biodegradable and carcinogenic are also considered as water pollutants, and various thermal, physical, chemical, electrical and biological methods have been applied for their treatment. A variety of sorbents [91,92] based on renewable resources have been reported in the literature. Table 1 summarizes maximum equilibrium sorption capacity hydrogels for heavy metal ions and ionic dyes.

3.5. Electroconductive hydrogels and biosensors

Electroconductive hydrogels (ECHs) are polymeric blends or co-networks that combine integrally Conductive Electroactive Polymers (CEPs) with vastly hydrated hydrogels. Electroconductive hydrogels belong to the general class of multifunctional smart materials (Fig. 11). As an emergent class, these materials seek to creatively combine the inherent properties of constituent materials, to give rise to technologically relevant properties for devices and systems as a biorecognition membrane layer in various biosensors. In one instance, an electroconductive hydrogel that was synthesized from a

Table 1
Maximum equilibrium sorption capacity hydrogels for heavy metal ions and ionic dyes.

	Metal ion	SD[a]	pH[b]	T[c]	$q_{max,}$	Ref.
Sorbent						
Semi-IPN PMAAm/CP	Fe^{2+}	10	–	25	0.178	[93]
Semi-IPN PMAAm/HPC	Cu^{2+}	20	–	25	0.2	[93]
Semi-IPN SA-g-PAA/PVP/GE	Ni^{2+}	2	5	30	3.158	[94]
Semi-IPN SA-g-PAA/PVP/GE	Zn^{2+}	2	5	30	3.035	[94]
Sequential-IPN poly(PEGDA)/PMAA	Pb^{2+}	2	5	30	2.913	[94]
Semi-IPN poly(PEGDA)/PMAA	Cd^{2+}	1	5	25	0.33	[94]
Anionic dyes						
Semi-IPN CS/(AAm-PEG macromer)	Methyl orange	0.6	–	25	185.24	[95]
Semi-IPN(NaAA-co HEMA/MBA)	Congo red	1	7	25	172	[96]
Semi-IPN Cs/(AAm-PEG macromer)	Acid red	0.6	–	25	342.54	[95]
Cationic dyes						
Semi-IPN Alg/PASP	Malachite green	2	–	25	300	[97]
Semi-IPN (AA-co-HEMA/MBA)/SA	Methyl violet	1	7	25	126.18	[96]
Semi-IPN AA/AM/n-BA/amylose	Crystal violet	0.2	7.4	25	35.02	[98]

[a] Sorbent dosage (g/L).
[b] q_{maxx} in mmol/g.
[c] Temperature in °C.

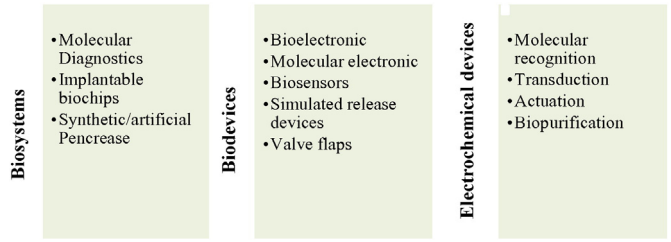

Fig. 11. Representation of biosensor applications.

poly(HEMA)-based hydrogel and poly(aniline) was fashioned into a biosensor by the incorporation of the recombinant cytochrome P450-2D6 [99]. This electroconductive hydrogel was subsequently fully characterized for its electrical, switching and optical properties, and demonstrated faster switching than its purely CEP counterpart. In another instance, an electroconductive hydrogel fashioned from poly(hydroxyethyl methacrylate) [poly(HEMA)] and polypyrrole (PPy) was investigated for its potential application in the clinically important biomedical diagnostic biosensors, by the incorporation of analyte-specific enzymes [99]. Among the various devices for which electroconductive hydrogel polymers were investigated are neural prosthetic and recording devices (NPDs and NRDs), electro-stimulated drug release devices (ESDRDs) [16–20] and implantable electrochemical biosensors [100]. In all cases these polymeric materials, which are both electronically and ionically conductive, provided a non-cytotoxic interface between the device and native living tissue or cell culture medium [101].

3.6. Agriculture industry

An attractive approach that has been more recently investigated involves the controlled release of nutrients from fertilizer-loaded hydrogels into crops. A large portion of the fertilizer applied to soil is lost by leaching, principally in highly porous soils, in chemical process, excessive rain and so on. A number of different polysaccharides, such as chitosan, pectin, and carboxymethyl cellulose [102] have been used to prepare hydrogels as a fertilizer release system to encourage the soil. Several authors have contributed to the application of hydrogel as soil conditioners. For instance, Agaba et al. [103] indicated that the moisture retention of a specific soil due to hydrogel is essential to a plantation forest establishment, as water influences soil properties such as aeration, temperature and nutrient transport, water uptake and transformation, which affect plant growth. Demitri et al. [104] investigated the applicability of cellulose-based hydrogels in three different formulations, i.e., crosslinked by carbodimide, as a carrier vehicle for sustained and controlled release of water and as nutrients in arid and desert areas. According to the authors, the main advantage is that the hydrogels may control the release of stored water as the soil dries, maintaining the soil humidity over a relatively long time. In addition, the presence of the hydrogel increases the soil porosity, providing better oxygenation to the plant roots. Parvathy and Jyothi [105] studied the effects of hydrogels on the physical–chemical and biological properties of the soil, based on the saponified cassava starch-g-poly(acrylamide). They also investigated the effects of the same hydrogel on the growth parameters of chili (*Capsicum annuum* L.) in different irrigation intervals. The results showed that the amount of moisture retained in the soil was dependent of the concentration of the superabsorbent matrices, which provide a better control of release of adsorbed water. They also indicated that these hydrogels are potential candidates to be applied as an alternative to combat global climate change because they can improve the soil properties, mainly in conditions of reduced moisture availability. They concluded that these matrices have excellent slow-release properties and good water retention capacity, indicating potential application in agriculture because they reduce the loss of fertilizers and improved the availability of water. A review paper [106] presented some polysaccharide-based controlled-release formulations including hydrogel matrices. According to the authors, the main advantages of polysaccharide over synthetic polymers are their eco-friendly source, high holding capacity, low-cost and biodegradability.

3.7. Contact lenses

Hydrogels are ideal candidates for the fabrication of micro optical arrays with dynamically tuneable focal lengths, which can be prepared in an inexpensive and scalable fashion. Methods of fabrication of micro lens arrays include photolithography, photo-thermal patterning and assembly of polymer particles, accompanied by their melting [107]. Such methods frequently require precise and several fabrication steps. Also, micro lens arrays are typically composed of optical elements with fixed focal lengths, in somewhat large diameters, and with slow speeds of focal length switching [108]. Also reported was the fabrication of ordered micro lens arrays via the electrostatically driven assembly of poly(NIPAM-AA) microgels on glass substrates functionalized with (3-aminopropyl)trimethoxysilane. At pH = 6.5 the electrostatic attraction between the anionic AA groups of the microgels and the amine groups on the substrate enabled binding of the particles to the surface. The lensing ability of the microgels spread on the substrate originated from their hemispherical shape, and the refractive index contrast between the contracted microgel and the medium. A higher refractive index contrast resulted in a lens with shorter focal length and improved lens power. More recently, [109] reported the fabrication of arrays of photoswitchable microlenses. These arrays were fabricated by depositing poly(NIPAM-AA) microgels onto the surface, coated with gold nanoparticles. The system was locally heated by irradiation at $\lambda = 532$ nm (the surface plasmon modes of the Au NPs). Plasmon excitation of the NPs resulted in energy transfer to the microgels in the form of heat to the microgel particles. The modulation of the focal length of the microlens arrays was investigated by their illumination with laser lights of various powers at different temperatures and pH. Enhanced focusing was achieved when the laser light excitation of the Au NPs resulted in microgel heating to a temperature greater than the VPTT of the poly(NIPAM-AA) microgels. Given their inherently fast volume transition, simple fabrication techniques, and the dynamic tunability of the focal length, the microgel-based microlens arrays are promising devices for the future development of micro-optics technology.

3.8. Food packaging industry

Several research groups as well as industrial companies worldwide are now developing new eco-friendly packaging solutions to exploit the 'ecological' advantages of biopolymers in applications such as food packaging. Biopolymers directly extracted from biomass (e.g., proteins, polysaccharides, lipids) or from microorganisms (e.g., polyhydroxyalkanoates), as well as some produced by classical chemical synthesis (e.g., polylactic acid) have been used to develop new structures for the development of food packaging applications from biopolymers, which has lagged behind medical materials due to high cost, low strength, and poor water resistance. Until recently, the most exploited routes to overcome these limiting factors involved blending natural and synthetic polymers together or incorporating inorganic fillers [110]. As an alternative, hydrogels can also offer new opportunities for the design of efficient biopolymer packaging materials with desirable properties. The specific nature of biopolymers critically influences the properties attainable from the complexes. Stiff and rigid linear polysaccharides such as pectin and xanthan gum, when mixed with proteins, tend to form complexes well-suited for producing gels in the form of sheets, membranes and coatings. In contrast, more globular and flexible

polysaccharides such as acacia gum generate spherical structures (e.g., micro- and nano-capsules) that can encapsulate active compounds and be embedded in films. Similarly, high molecular weight-flexible proteins are the most suitable for the development of protein-polysaccharide pairs, due to the capability of withstanding the changes in the biopolymer conformation involved in the different types of associations (i.e., electrostatic, hydrophobic, physical entanglements) [111]. As shown in Table 2, different protein-polysaccharide combinations have been recently reported for food packaging applications, each one with specific advantages and disadvantages. Promising applications of hydrogels in food packaging industries include improved packaging (gas and moisture barriers), antibacterial packaging, product condition monitoring, nanoadditives, enhanced shelf life, protection from oxidation and task masking.

3.9. Cosmetic industry

The continuous development of new active ingredients for cosmetics and personal care products is one of the most important areas of research in this industry [121]. There are a significant number of novel cosmetic products based on this new generation of active ingredients [122]. Chitosonic® Acid and carboxymethyl hexanoyl chitosan are novel chitosan-based materials that have recently been accepted by the Personal Care Products Council as a new cosmetic ingredients with the INCI (International Nomenclature of Cosmetic Ingredients) name Carboxymethyl Caprooyl Chitosan. Although some articles have reported that chitosan and its derivatives can be used as a delivery system for cosmetics [80], to the best of the author's knowledge, no studies have demonstrated that chitosan and its derivatives can be used as key active ingredients in the formulation of cosmetics. Therefore, this review reports several important characteristics and activities of Chitosonic® Acid (Fig. 12), including the average molecular weight, solubility in water, zeta-potential, isoelectric point, hydrophilic–lipophilic balance (HLB) value, and the antimicrobial, antioxidant and hydration activities. Moreover, the cytotoxicity of Chitosonic® Acid to mouse fibroblast L-929 cells has been studied to determine its safety. Such findings propose that this chitosan derivative may be used as an active ingredient in cosmetic products.

In summary, the novel cosmetic ingredient Chitosonic® Acid is a water-soluble chitosan derivative with a high HLB value. Chitosonic® Acid can form a nano-network structure when its concentration is higher than 0.5% and can self-assemble into a nanosphere structure when its concentration is lower than 0.2%. Chitosonic® Acid has potent antimicrobial activities against gram-positive bacteria, gram-negative bacteria and fungus. Chitosonic® Acid also has moderate DPPH radical scavenging activity. Additionally, Chitosonic® Acid exhibits good hydration activity for absorbing and retaining water molecules. From a safety point of view, Chitosonic® Acid has no cytotoxicity to L-929 cells if its concentration is less than 0.5%. Moreover, Chitosonic® Acid has good compatibility with many ingredients that are commonly used in cosmetics.

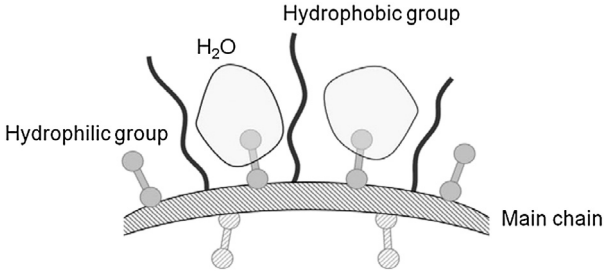

Fig. 12. Illustration of the interaction between water and Chitosonic® Acid molecules [80].

3.10. Enhanced in oil recovery

Excess water production is a frequent problem that occurs in advanced reservoirs as a result of long-term water flooding, which usually results in increased levels of corrosion and scale, increased environmental concerns, and ultimately leads to early shut-in of the wells that still contain significant volumes of hydrocarbons [123]. In an attempt to mitigate excess water production and hence increase hydrocarbon production, hydrogels are often injected near the wellbore to preferentially seal the higher permeability zones or fractures, thus diverting the injected water into low permeability upswept hydrocarbon-rich zones [95]. In prior experiments, several unsuccessful attempts were made to disperse polymer in clay by a simple magnetic stirring. Thus, in the solution, the electrostatic attraction between the edges and the surface of the different clay discs (rim–face interactions) causes the formation of tactoids or “house of cards”, preventing the adequate dispersion of clay into the solution and hence, an inadequate intercalation of polymer in the clay network. Several considerations were made to chemically modify the surface charges of the clay, making both surface and edge negatively charged, and thereby favouring clay–clay repulsion and hence obtaining better clay dispersion in the solution. After further consideration, the authors finally settled on the utilization of a high shear mixer, which provides sufficient energy to completely shear clay platelets apart, forming exfoliated nanostructures, which form a temporary dispersion until the polymer is introduced and crosslinking occurs, forming a three-dimensional gel network. To understand the behaviour and characteristics demonstrated by the nanocomposite gel, it is necessary to postulate a mechanism illustrating the interaction between the polymer and clay as shown in Fig. 13. Based on the proposed model, the negatively charged polymer chains bind to the positively charged edges of the clay (polymer–rim interactions). This is further enhanced by the formation of hydrogen bond interactions between the oxygen atoms in clay and the hydrogen atoms in the amide side chain of the polymer, as well as the complexation of metal ions on the clay surface with carboxylate oxygen atom of the polymer. Consequently, the nanocomposite gel exhibits a remarkable mechanical performance, suitable for use in controlling excess water production through profile modification, and as water shut-off agents during enhanced oil recovery operations.

Table 2
Protein–polysaccharide combinations for the production of composite structures.

Hydrogels	Application	Form	Method	Advantage/disadvantage	Ref.
Beta-lactoglobulin/pectin	Food wrapping	Films	Electrostatic association	Colloidal stability, transparent dispersion	[112]
Starch/cellulose	Food packaging	Films	Air-drying casting	High tensile strength/poor optical properties	[113]
Chitosan/pectin	Coating for crop protection	coatings	Dipping	Antimicrobial/high coating thickness	[114]
Gelatin–alginate	Edible casting	Films	Extrusion	Oxygen barrier/turbidity	[115]
Chitosan/gelatin	Antimicrobial packaging	Coatings	Solvent-casting	Antimicrobial/dissolvable	[116]
Gelatin/pectin	Food covering	Films	Air-drying casting	High transparency	[117]
Methylcellulose/whey protein	Moisture sensitive packaging	Films	Air-drying casting	Water vapour/phase separation barrier	[118]
Zein/starch	Inner packaging	Films	Doping starch in zein sol.	Water vapour transmission/poor flexibility	[119]
Gelatin/cane bagasse	Self-fertilizing biofilms	Films	Air-drying casting	Thermal stability, rigidity, dark colour	[120]

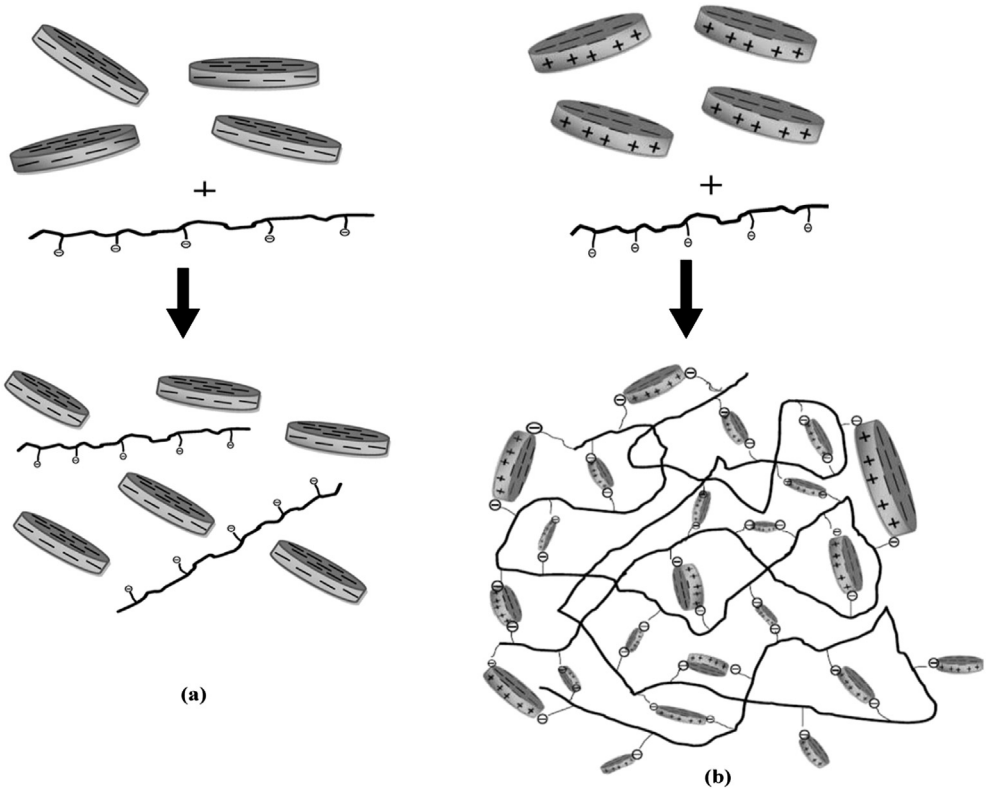

Fig. 13. Anionic–anionic polymer/clay repulsions results in no gelation. (b) Gelation occurs due to electrostatic interaction between anionic polymer and cationic clay surface [124].

3.11. Technical features of hydrogels

The technical features of hydrogels are listed as follows:

- Utmost stability and constancy in a swelling environment and during storage;
- Utmost absorption ability (maximum equilibrium swelling) in brine;
- Preferred rate of absorption, particle size and porosity;
- pH-neutral, colourless, odourless and absolutely non-toxic;
- The highest absorbency under load (AUL);
- Photo stability, low soluble content and residual monomer and low price;
- Re-wetting capability (if required) — the hydrogel has to be able to give back the imbibed solution or maintain it as needed, (e.g., in agricultural or hygiene applications);
- Maximum biodegradability without formation of toxic groups.

In the light of the above features, it is not possible to produce a hydrogel with all the technical features, although some properties can be achieved like porosity, response to either pH or temperature, use in drug delivery and the sanitized product of hydrogels that must possess the lowest re-wetting, the highest absorption rate and the lowest residual monomer. Table 3 details the general properties of natural, synthetic polymers and nano-composites.

4. Process design implications

Polymeric hydrogels are normally produced by one of two well-established schemes

- Polymerization of hydrophilic monomers; or
- Modification or functionalization of existing polymers (natural or artificial).

The unique sources of hydrogels is comprised of two main classes, i.e., natural, containing two main groups based on polypeptides (proteins) and polysaccharides, and another is artificial (petrochemical-based). Natural-hydrogels are usually prepared through the addition of some synthetic parts onto the natural substrates, e.g., graft copolymerization of vinyl monomers on polysaccharides. When the term "hydrogel" is used without specifying its type, it truly means the conventional type of hydrogel [134]. The synthetic route for the production of most synthetic hydrogels is the free-radical multifunctional vinyl monomers. Each monomer contains a carbon double bond where an active centre may propagate to produce polymer chains. But, generating active centres also depends on the solvents, reaction conditions and particular monomers and can be initiated by heat (thermal-initiators), light (photo-initiators), enzymes (bio-initiators) or electron beams [135] as shown in Fig. 14.

Usually, water-soluble natural or synthetic polymers are crosslinked to form hydrogels in a number of ways, such as (1) linking polymer chains via chemical reaction, (2) using ionizing radiation to generate main-chain free radicals, which can recombine as crosslink joints, and (3) interacting physically such as electrostatics, entanglements and crystallite interactions.

Any of the various polymerization techniques can be used to form hydrogels, including bulk, solution and suspension polymerizations. The three main components of hydrogels are monomers, initiators and crosslinkers, which can be diluted in water or any solvent to control the heat of polymerization. However, its disadvantage appears in the form of impurities left from the preparation process containing unreacted monomers, initiators, crosslinkers and side products. Hydrogels are commonly prepared from polar monomers of both natural and synthetic origins by graft polymerization, crosslinking polymerization, network formation in aqueous medium and by radiation crosslinking methods. The various polymerization techniques for the production of hydrogels are described as follows.

Table 3
Properties of natural, synthetic polymers and nano-composites.

Type	Properties	Ref.
Natural polymer		
Alginate	Biocompatible and biodegradable polymer; suitable for in situ injection; crosslinking is under very mild conditions; water soluble polymer; mechanical weakness; difficulties in handling, storage in solution, and sterilization	[125]
Chitosan	Excellent biocompatibility and good host response; unique biodegradability by lysozyme and other enzymes; high antimicrobial activity; hydrophilic surface provides easy cell adhesion, proliferation and differentiation; mechanical weakness; very viscous polymer solution; water soluble-polymer only in acetic medium; high purification cost	[126]
Starch	Water soluble polymer; inexpensive; in vivo biodegradable; biocompatible; easy to modify with other polymers; difficulties in crosslinking itself; mechanical weakness; needs modification to enhance cell adhesion	[127]
Dextran	Water soluble polymer; in vivo biodegradable by a-amylase; biocompatible; good proliferation and differentiation behaviour; expensive polymer; mechanical weakness; needs modification to enhance cell adhesion	[126]
Glucan	Water soluble polymer, but yeast-glucan is not soluble in water; biocompatible-biodegradable polymer; has excellent antibacterial and antiviral activities; fast wound healing rate	[128]
Gelatin	Water-soluble polymer; obtained from various animal by-products; forms thermally-revisable and high mechanical hydrogels; widespread in biomedical application; easily forms films and matrix hydrogels; very viscous polymer solution; very fast biodegradation; lower thermal stability at high temperatures	[129]
Synthetic polymers		
PNIPAAM	Water soluble polymer; temperature-responsive polymer; good mechanical properties; biocompatible polymer for tissue engineering and controlled drug delivery; needs chemical crosslinking; needs modification to enhance culture surface for cell delivery; somewhat cytotoxic; significantly lower thermal stability	[130]
PVP	Water soluble polymer; excellent wetting properties; swells rapidly; excellent film; non-toxic; biocompatible; wide application in blood plasma expander polymer; high storage stability; mechanical weakness; lower thermal stability	[131]
Polymer-composite		
(MMT) clay	Natural inorganic clay and hydrophilic in nature; needs modification and intercalation reaction before use; forms high mechanical and thermal resistance nanocomposite hydrogels with enhanced cell adhesion and non-biodegradable nano or micro-particles	[132]
ZnO nanoparticles	Inorganic nanoparticles; insoluble in water; have been used for medicine e.g., skin condition powder, and for industrial e.g., portable energy, sensors, wallpapers and film formation; excellent antibacterial activity at low concentrations; toxic at high concentrations; non-biodegradable	[133]

4.1. Solution polymerization of hydrogel

In solution polymerization, the neutral or ionic monomers are crosslinked with a multifunctional crosslinking agent in the presence of a thermal, redox or UV initiator. The major advantage of solution polymerization over bulk polymerization is the presence of the solvent serving as heat sink. The prepared hydrogels need to be washed with distilled water to get rid of undesired monomers, initiators and crosslinkers. Typical solvents used in this method include water, ethanol, a mixture of water and ethanol, and benzyl alcohol.

Free-radical initiated polymerization of acrylic acid (AA) and its salts by a crosslinker, e.g., methylene bis-acrylamide (MBA), is frequently used and is a straight forward process for hydrogel preparation by solution polymerization [2,137]. Briefly, the reactants are dissolved in water at the desired concentrations, usually about 10–70%. Groups like carboxylic acid of the product are neutralized partially before or after the polymerization. In this process, the initiation is usually carried out by the reaction of a reducing agent with an oxidizing agent (redox system), or chemically with a free-radical azo or peroxide thermal dissociative species. A fast exothermic reaction yields a gel-like elastic product, which is dried, and the macro-porous mass is ground and sieved to get the required particle size [138]. This preparative method is usually very sensitive to handle due to the lack of sufficient reaction control, a rubbery or solid reaction product, mono/poly-dispersity and an increase the in the sol content mainly due to uncontrolled thermal and hydrolytic cleavage. However, as it is a faster technique, less expensive, and has suitable swelling properties, this method is preferred for laboratory and industrial scale as shown in Fig. 15.

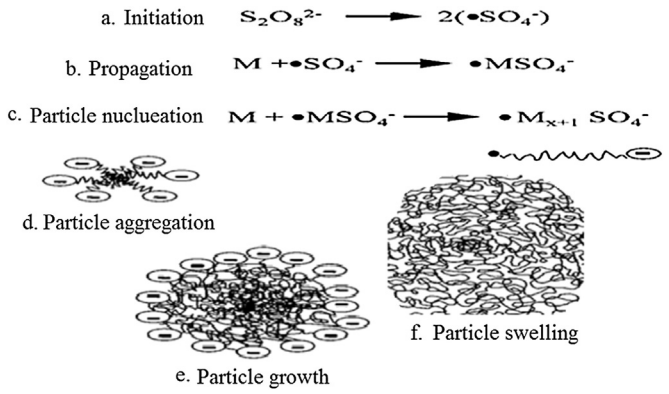

Fig. 14. Mechanism of preparing hydrogels by free radical polymerization [136].

4.2. Suspension polymerization

In suspension polymerization, the monomer solution is allowed to disperse in the non-solvent resulting in fine monomer droplets, which

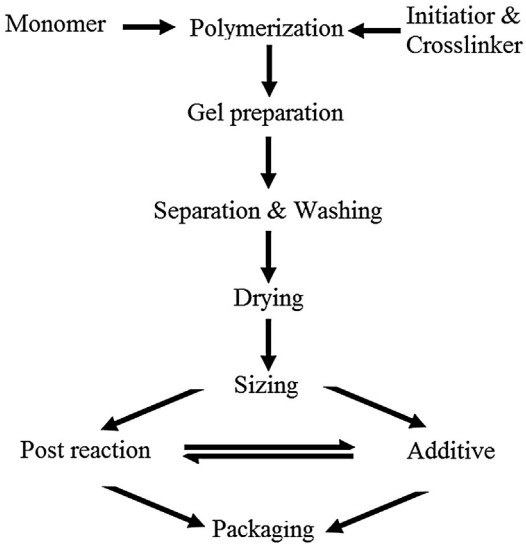

Fig. 15. Hydrogel synthesis by solution polymerization [136].

are stabilized by the addition of a stabilizer. The process is initiated by radicals due to the thermal decomposition of the initiator. Thus, the formed product is then washed to remove unreacted monomers, initiators and crosslinking agents. Recently, for polyacrylamide-based hydrogels [139], the inverse-suspension technique was widely used due to its easy removal and supervision of the risky, residual acrylamide monomer in the polymer. A free-radical suspension polymerization of 2-hydroxyethyl methacrylate (HEMA) lightly crosslinked with ethylene glycol dimethacrylate (EGDMA) was reported [140].

The inverse-suspension, a more versatile system with high swelling capacity and fast absorption kinetics, has been applied [141]. When the initiator dissolves in the dispersed (aqueous) phase, each particle contains all the reactive species. Therefore, each behaves like an isolated micro-batch polymerization reactor, which is easily removed by centrifugation or filtration. Hence, the inverse-suspension method displays supplementary advantages compared to the solution method, like control of the reaction heat elimination, regulation of mono/poly-dispersity and modification of the particle size [142]. Fig. 16 shows that the suspension polymerization process is very similar to the solution polymerization process, but with maximum yield, a narrow distribution size, smoothness, sphericity, clarity, as well as reduced formation of undesirable fine particles.

4.3. SAPs and SPHs

Superabsorbent polymers (SAPs) are an innovative class of hydrogel products [143,144], which were introduced in agriculture, diaper and other industries where excellent water holding properties are of major importance. In 1998, super porous hydrogels (SPHs) were considered a different category of water-absorbent polymer systems with enhanced mechanical and elastic properties, capable of absorbing water 10–1000 times their original weight or volume in a short time [138]. Super porous hydrogels are prepared using several techniques, such as phase separation, freeze-drying, micro-emulsion and gas blow techniques [13,138,145]. Using the same monomer solution (Fig. 17), different types of networks, such as porous, non-porous and super porous structures have been reported by using foam stabilizers, foaming aids and foaming agents [13].

4.3.1. SAPs vs. SPHs

The SPHs swell immediately upon contact with water, regardless of their size in the dried state. The initial wetting of SAP particles is slower than that of SPHs, and the fast swelling is based on the small size of the SAP particles. If SAPs were made into bigger size samples, swelling would not be as fast as with their smaller counterparts. The unique properties of the size-independent fast-swelling kinetics of SPHs are accounted for by their interconnected open cellular structure. The open porous structure allows extremely fast absorption of water into

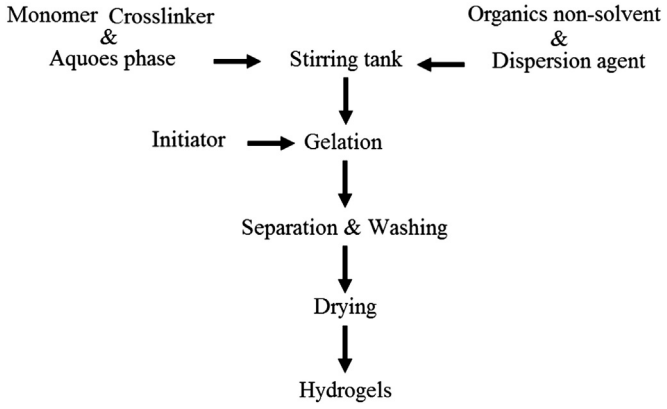

Fig. 16. Hydrogel synthesis by suspension polymerization [141].

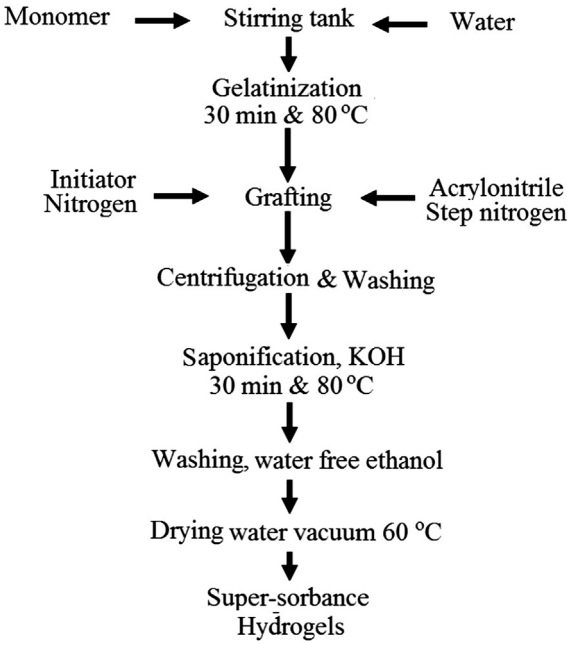

Fig. 17. Preparation of superabsorbent hydrogel [134].

the centre of the dried matrix by capillary force. The same monomer solution can produce different types of water-absorbing polymer networks, such as non-porous, porous and super porous structures, depending on the presence of a foaming agent, which can in turn be stabilized using poly(ethylene oxide)–poly(propylene oxide)–poly(ethylene oxide) (PEO–PPO–PEO) triblock copolymers as surfactants. The reaction profile can significantly affect the swelling and physical properties of the final product due to the different oxygen interferences [146].

4.3.2. 1st generation SPHs: conventional SPHs

The most commonly used monomers for synthesis of the first generation of SPHs are highly hydrophilic acrylamide, salts of acrylic acid and sulfopropyl acrylate. Although dried SPHs are inelastic and stiff, its hydrophilic nature results in moisture-induced plasticization of the inflexible structures into soft and elastic structures. The dried SPHs swell fast to a large size, larger than a few hundred times of their own volume in a dried state. Due to the extremely small fraction of the polymer in a swollen state, the swollen SPHs are sometimes difficult to handle without breaking. When the SPHs dry, the porous structure collapses or shrinks due to the surface tension of the water pulling the polymer chains together during the drying process. To avoid this problem, the water inside SPHs is replaced with alcohol (e.g., ethanol). The low surface tension of the alcohol prevents the porous structure from collapsing during drying. The CSPHs are fragile against bending or tensile stresses. Their structures are easily broken apart even under very low pressure. The lack of desirable mechanical properties in the conventional SPHs triggered the development of the second-generation SPH composites.

4.3.3. 2nd generation SPHs: SPH composites

A composite is the matrix of a continuous phase that has a dispersed phase incorporated within. Composite structures are generally made to attain certain properties, which cannot otherwise be achieved by each matrix alone. For making SPH composites, a matrix-swelling additive or a composite agent is utilized. A composite agent used in SPH composites is a crosslinked water-absorbent hydrophilic polymer that can absorb the solution of monomer, crosslinker, initiator and remaining components of the SPH synthesis. Upon polymerization, the composite agent serves as the local point of physical crosslinking (or

entanglement) of the formed polymer chains. During the polymerization process, each composite agent particle acts as an isolated individual reactor in which crosslinking polymerization occurs. As the crosslinking polymerization proceeds throughout the solution, individual swollen composite agent particles are connected together through polymer chains connecting them. The presence of composite agents in the SPH composites result in improved mechanical properties compared to the conventional (i.e., the first generation) SPH, but the SPH composites are still brittle and thus break into pieces upon application of stress. This modification over conventional SPHs resembles modification of superabsorbent polymers through surface crosslinking. Overall, this type of modification results in a higher modulus polymer network in the swollen state, which is susceptible to failure under the brittle fracture mechanism.

4.3.4. 3rd generation SPHs: SPH hybrids

To synthesize SPHs with very high mechanical or elastic properties, the third generation of SPH was developed based on SPH hybrids. Unlike SPH composites wherein a pre-crosslinked matrix-swelling additive is added, SPH hybrids are prepared by adding a hybrid agent that can be crosslinked after the SPH is formed. The hybrid agent is a water-soluble or water-dispersible polymer that can form crosslinked structures (in a manner similar to forming interpenetrating networks) through chemical or physical crosslinking. Examples of hybrid agents are polysaccharides, including sodium alginate, pectin, chitosan and synthetic water-soluble hydrophilic polymers such as poly(vinyl alcohol). Once the second network is formed, the whole system becomes similar to interpenetrating polymer networks. An example of SPH hybrids is the synthesis of acrylamide-based SPH in the presence of sodium alginate, followed by the crosslinking of alginate chains by calcium ions. One of the unique properties of SPH hybrids is that the gels are highly elastic in the swollen state. As compared with conventional SPHs and SPH composites, SPH hybrids are not easily breakable when stretched. The elastic and rubbery properties make the SPH hybrids a choice for various applications where resilient gels are preferred. The resiliency of the fully water-swollen SPHs has never been observed previously. Elastic water-swollen SPH hybrids can resist various types of stresses, including tension, compression, bending and twisting. The SPH hybrid (SPHH) of alginate polyacrylamide could withstand compression forces of up to 25 N, while its SPH composite (SPHC) counterpart (crosslinked carboxymethyl cellulose-polyacrylamide) failed under a 2 N force. The mechanical property of the first-generation polyacrylamide SPH was not sufficient under testing conditions to be evaluated by the mechanical tester.

For the production of SPHs, redox couple initiators such as ammonium persulphate/sodium metabisulphite or potassium persulphate/sodium metabisulphite are used, while SAPs are produced using thermal and redox systems both by crosslinking polymerization, also called gelation and foaming, which need to be conducted in such a way to enable matched foaming and gelation. As no foam stabilizer is used during the preparation of the SAPs, it results in uncontrolled pore sizes. However, this problem can be overcome during dehydration using ethanol, which helps to stabilize the product and prevents it from shrinking and dehydrating totally to result in a white solid, brittle and porous product. The formulations to prepare SAPs and SPHs are summarized in Table 4.

4.3.5. New generations of SPHs

The fact that SPHs absorb water very fast, even in large quantities, makes them useful in the development of physiological platforms. The fully swollen SPHs, however, are mechanically very poor to meet the requirements of certain applications for which a very high mechanical property (in their swollen state) is highly demanded. To distinguish SPHs with different properties, the SPHs are divided into three different generations. The conventional (i.e., the first generation) SPH is characterized as fast swelling, with high swelling ratio and weak mechanical properties. On the other hand, the second-generation SPH (SPH composites) is characterized as fast swelling, with medium swelling ratio and improved mechanical properties. The third-generation SPH hybrid (SPHHs) possesses elastic properties that can be highly useful in biomedical developments, as well as other pharmaceutical and industrial applications.

Table 4
Formulations of SAPs and SPHs' preparation [13].

Starting material	Role	Nonporous SAP	Porous SAP	SPH
Acrylamide, acrylic acid	Monomer	√	√	√
Bis-acrylamide	Crosslinker	√	√	√
Deionized water	Solvent	√	√	√
Ammonium persulphate	Oxidant	√	√	√
Tetramethyl ethylenediamine	Reductant	√	√	√
Glacial acetic acid	Foaming aid		√	√
Sodium bicarbonate	Foaming agent		√	√
PEO–PPO–PEO block copolymers	Foam stabilizer		√	√
Starting reaction temperature °C		25 °C	25 °C	25 °C
Reaction product after synthesis		Solid rigid	Unstable foam	
Swelling capacity (g/g)		9	20	33
Swelling retardation period (min)		185	55	1

5. Conclusions and perspectives

This review demonstrates the literature in the field of hydrogels in the past 20 years, which describe the classification of hydrogels based on the different physical and chemical properties with emphasis on stimuli responsive hydrogels for biomedical, environmental and industrial applications. The method of preparing hydrogels and the designing process influence the production of hydrogels by different techniques, where a high degree of sensitivity is required and explained. The path of the research in this review indicates that the combination of polymers, which responds to different stimuli (physical, chemical and biochemical) must be identified and future generations of hydrogel that undergo spontaneous swelling when in contact with lungs and cancer cells should be investigated. An innovative category, which is environmentally friendly, called SAPs and SPHs are new materials that swell rapidly to a large size regardless of their original size and show remarkable properties, diplomacy and are recognizable with particular consideration. The materials tend to absorb much water or aqueous fluids in a relatively short period. This innovative category will receive serious attention from researchers in ion impregnated and modified selectivity in the future. In this age of nanofabrication, there is a need for miniaturization of these hydrogels with enhanced durability, mechanical properties and biocompatibility for new applications. Therefore, realizing the clinical requirements and simultaneously limiting the complexity of the hydrogel formulation will be the main goal for the coming decades.

Acknowledgements

The authors wish to acknowledge the Universiti Sains Malaysia for sponsoring the project under USM-FRGS-6071242 and USM-RU-PGRS 8046027, as well as the School of Material and Mineral Source Engineering and the USM Engineering Campus for their technical support. The first author is highly grateful to The World Academy of Sciences (TWAS, for the advancement of science in developing countries) and USM for a TWAS-USM PhD fellowship.

References

[1] J.M. Rosiak, F. Yoshii, Hydrogels and their medical applications, Nucl. Instrum. Methods Phys. Res., Sect. B 151 (1999) 56–64.
[2] E.A. El-Hefian, E.S. Elgannoudi, A. Mainal, A.H. Yahaya, Characterization of chitosan in acetic acid: rheological and thermal studies, Turk. J. Chem. 34 (2010) 47–56.

[3] A. Khan, M.B.H. Othman, K.A. Razak, H.M. Akil, Synthesis and physicochemical investigation of chitosan-PMAA-based dual-responsive hydrogels, J. Polym. Res. 20 (2013) 1–8.
[4] O. Wichterle, D. Lim, Hydrophilic gels for biological use, Nature 185 (1960) 117–118.
[5] N. Peppas, P. Bures, W. Leobandung, H. Ichikawa, Hydrogels in pharmaceutical formulations, Eur. J. Pharm. Biopharm. 50 (2000) 27–46.
[6] S.A. Dergunov, G.A. Mun, γ-Irradiated chitosan-polyvinyl pyrrolidone hydrogels as pH-sensitive protein delivery system, Radiat. Phys. Chem. 78 (2009) 65–68.
[7] M.J. Park, S.M. Hur, H.K. Rhee, Online estimation and control of polymer quality in a copolymerization reactor, AICHE J. 48 (2002) 1013–1021.
[8] I. Gibas, H. Janik, Review: synthetic polymer hydrogels for biomedical applications, Chem. Chem. Technol. 4 (2010) 297–304.
[9] F. Ganji, S. Vasheghani-Farahani, E. Vasheghani-Farahani, Theoretical description of hydrogel swelling: a review, Iran. Polym. J. 19 (2010) 375–398.
[10] N. Das, Preparation methods and properties of hydrogel: a review, Int. J. Pharm. Pharm. Sci. 5 (2013) 112–117.
[11] A.S. Hoffman, Hydrogels for biomedical applications, Adv. Drug Deliv. Rev. 64 (2012) 18–23.
[12] E.M. Ahmed, Hydrogel: preparation, characterization, and applications, J. Adv. Res. 6 (2013) 105–121.
[13] J. Kuang, K.Y. Yuk, K.M. Huh, Polysaccharide-based superporous hydrogels with fast swelling and superabsorbent properties, Carbohydr. Polym. 83 (2011) 284–290.
[14] Y. Qiu, K. Park, Environment-sensitive hydrogels for drug delivery, Adv. Drug Deliv. Rev. 53 (2001) 321–339.
[15] H.-P. Cong, P. Wang, S.-H. Yu, Stretchable and self-healing graphene oxide–polymer composite hydrogels: a dual-network design, Chem. Mater. 25 (2013) 3357–3362.
[16] M. Yalpani, Polysaccharides: Syntheses, Modifications and Structure/Property Relations, Elsevier, New York, 2013.
[17] B. Thu, P. Bruheim, T. Espevik, O. Smidsrød, P. Soon-Shiong, G. Skjåk-Bræk, Alginate polycation microcapsules: I. Interaction between alginate and polycation, Biomaterials 17 (1996) 1031–1040.
[18] X. Shu, K. Zhu, A novel approach to prepare tripolyphosphate/chitosan complex beads for controlled release drug delivery, Int. J. Pharm. 201 (2000) 51–58.
[19] N. Annabi, K. Tsang, S.M. Mithieux, M. Nikkhah, A. Ameri, A. Khademhosseini, A.S. Weiss, Highly elastic micropatterned hydrogel for engineering functional cardiac tissue, Adv. Funct. Mater. 23 (2013) 4950–4959.
[20] W. Hennink, C. Van Nostrum, Novel crosslinking methods to design hydrogels, Adv. Drug Deliv. Rev. 64 (2012) 223–236.
[21] Y. Zhang, F. Wu, M. Li, E. Wang, pH switching on-off semi-IPN hydrogel based on cross-linked poly(acrylamide-co-acrylic acid) and linear polyallyamine, Polymer 46 (2005) 7695–7700.
[22] B. Baroli, Photopolymerization of biomaterials: issues and potentialities in drug delivery, tissue engineering, and cell encapsulation applications, J. Chem. Technol. Biotechnol. 81 (2006) 491–499.
[23] Y. Garcia, R. Collighan, M. Griffin, A. Pandit, Assessment of cell viability in a three-dimensional enzymatically cross-linked collagen scaffold, J. Mater. Sci. Mater. Med. 18 (2007) 1991–2001.
[24] P. Gupta, K. Vermani, S. Garg, Hydrogels: from controlled release to pH-responsive drug delivery, Drug Discov. Today 7 (2002) 569–579.
[25] Z. Wang, X. Hou, Z. Mao, R. Ye, Y. Mo, D.E. Finlow, Synthesis and characterization of biodegradable poly (lactic acid-co-glycine) via direct melt copolymerization, Iran. Polym. J. 17 (2008) 791–798.
[26] T. Iizawa, H. Taketa, M. Maruta, T. Ishido, T. Gotoh, S. Sakohara, Synthesis of porous poly (N-isopropylacrylamide) gel beads by sedimentation polymerization and their morphology, J. Appl. Polym. Sci. 104 (2007) 842–850.
[27] J. Lim, A. Chouai, S.-T. Lo, W. Liu, X. Sun, E.E. Simanek, Design, synthesis, characterization, and biological evaluation of triazine dendrimers bearing paclitaxel using ester and ester/disulfide linkages, Bioconjug. Chem. 20 (2009) 2154–2161.
[28] C. Gong, S. Shi, P. Dong, B. Kan, M. Gou, X. Wang, X. Li, F. Luo, X. Zhao, Y. Wei, Synthesis and characterization of PEG–PCL–PEG thermosensitive hydrogel, Int. J. Pharm. 365 (2009) 89–99.
[29] J.-T. Zhang, R. Bhat, K.D. Jandt, Temperature-sensitive PVA/PNIPAAm semi-IPN hydrogels with enhanced responsive properties, Acta Biomater. 5 (2009) 488–497.
[30] Y.S. Lipatov, Polymer blends and interpenetrating polymer networks at the interface with solids, Prog. Polym. Sci. 27 (2002) 1721–1801.
[31] G.-S. Liou, P.-H. Lin, H.-J. Yen, Y.-Y. Yu, T.-W. Tsai, W.-C. Chen, Highly flexible and optical transparent 6F-PI/TiO_2 optical hybrid films with tunable refractive index and excellent thermal stability, J. Mater. Chem. 20 (2010) 531–536.
[32] D. de Britto, S.P. Campana-Filho, Kinetics of the thermal degradation of chitosan, Thermochim. Acta 465 (2007) 73–82.
[33] E.S. Gil, S.M. Hudson, Stimuli-responsive polymers and their bioconjugates, Prog. Polym. Sci. 29 (2004) 1173–1222.
[34] S.I. Kang, Y.H. Bae, A sulfonamide based glucose-responsive hydrogel with covalently immobilized glucose oxidase and catalase, J. Control. Release 86 (2003) 115–121.
[35] N. Kashyap, N. Kumar, M.R. Kumar, Hydrogels for pharmaceutical and biomedical applications, Crit. Rev. Ther. Drug Carrier Syst. 22 (2005) 107–150.
[36] A. Patel, K. Mequanint, Hydrogel biomaterials, Biomedical Engineering—Frontiers and ChallengesCap, 142011 275–296.
[37] E. Jabbari, S. Nozari, Synthesis of acrylic acid hydrogel by gamma-irradiation cross-linking of polyacrylic acid in aqueous solution, Iran. Polym. J. 8 (1999) 263–270.
[38] F. Jianqi, G. Lixia, PVA/PAA thermo-crosslinking hydrogel fiber: preparation and pH-sensitive properties in electrolyte solution, Eur. Polym. J. 38 (2002) 1653–1658.
[39] J. Li, X. Li, X. Ni, X. Wang, H. Li, K.W. Leong, Self-assembled supramolecular hydrogels formed by biodegradable PEO–PHB–PEO triblock copolymers and alpha-cyclodextrin for controlled drug delivery, Biomaterials 27 (2006) 4132–4140.
[40] J.P. Baker, D.R. Stephens, H.W. Blanch, J.M. Prausnitz, Swelling equilibria for acrylamide-based polyampholyte hydrogels, Macromolecules 25 (1992) 1955–1958.
[41] Y.-C. Nho, S.-E. Park, H.-I. Kim, T.-S. Hwang, RETRACTED: oral delivery of insulin using pH-sensitive hydrogels based on polyvinyl alcohol grafted with acrylic acid/methacrylic acid by radiation, Nucl. Instrum. Methods Phys. Res., Sect. B 236 (2005) 283–288.
[42] A. Ariffin, M.S. Musa, M.B.H. Othman, M.A.A. Razali, F. Yunus, Effects of various fillers on anionic polyacrylamide systems for treating kaolin suspensions, Colloids Surf. A Physicochem. Eng. Asp. 441 (2014) 306–311.
[43] F. Bossard, T. Aubry, G. Gotzamanis, C. Tsitsilianis, pH-tunable rheological properties of a telechelic cationic polyelectrolyte reversible hydrogel, Soft Matter 2 (2006) 510–516.
[44] T. Dolatabadi-Farahani, E. Vasheghani-Farahani, H. Mirzadeh, Swelling behaviour of alginate-N, O-carboxymethyl chitosan gel beads coated by chitosan, Iran. Polym. J. 15 (2006) 405.
[45] M. Sadeghi, H. Hosseinzadeh, Synthesis of starch—poly(sodium acrylate-co-acrylamide) superabsorbent hydrogel with salt and ph-responsiveness properties as a drug delivery system, J. Bioact. Compat. Polym. 23 (2008) 381–404.
[46] A. Richter, Hydrogels for actuators, Hydrogel Sensors and Actuators, Springer, Dresden, 2010 221–248.
[47] W.A. Laftah, S. Hashim, A.N. Ibrahim, Polymer hydrogels: a review, Polym.-Plast. Technol. Eng. 50 (2011) 1475–1486.
[48] L. Serra, J. Doménech, N.A. Peppas, Drug transport mechanisms and release kinetics from molecularly designed poly (acrylic acid-g-ethylene glycol) hydrogels, Biomaterials 27 (2006) 5440–5451.
[49] C. Gong, T. Qi, X. Wei, Y. Qu, Q. Wu, F. Luo, Z. Qian, Thermosensitive polymeric hydrogels as drug delivery systems, Curr. Med. Chem. 20 (2013) 79–94.
[50] L. Klouda, A.G. Mikos, Thermoresponsive hydrogels in biomedical applications, Eur. J. Pharm. Biopharm. 68 (2008) 34–45.
[51] M. Qiao, D. Chen, X. Ma, H. Hu, Sustained release of bee venom peptide from biodegradable thermosensitive PLGA–PEG–PLGA triblock copolymer-based hydrogels in vitro, Pharm. Int. J. Pharm. Sci. 61 (2006) 199–202.
[52] M. Behl, J. Zotzmann, A. Lendlein, Shape-memory polymers and shape-changing polymers, Shape-Memory Polymers, Springer, New York, 2010 1–40.
[53] Y. Wang, S. Xu, T. Chen, H. Guo, Q. Liu, B. Ye, Z. Zhang, Z. He, S. Cao, Synthesis and preliminary photovoltaic behavior study of a soluble polyimide containing ruthenium complexes, Polym. Chem. 1 (2010) 1048–1055.
[54] Y. Qiu, K. Park, Environment-sensitive hydrogels for drug delivery, Adv. Drug Deliv. Rev. 64 (2012) 49–60.
[55] H. Katono, A. Maruyama, K. Sanui, N. Ogata, T. Okano, Y. Sakurai, Thermo-responsive swelling and drug release switching of interpenetrating polymer networks composed of poly(acrylamide-co-butyl methacrylate) and poly(acrylic acid), J. Control. Release 16 (1991) 215–227.
[56] L.M. Geever, C.C. Cooney, J.G. Lyons, J.E. Kennedy, M.J. Nugent, S. Devery, C.L. Higginbotham, Characterisation and controlled drug release from novel drug-loaded hydrogels, Eur. J. Pharm. Biopharm. 69 (2008) 1147–1159.
[57] Z. Li, J. Guan, Thermosensitive hydrogels for drug delivery, Expert Opin. Drug Deliv. 8 (2011) 991–1007.
[58] K. Podual, F. Doyle Iii, N. Peppas, Preparation and dynamic response of cationic copolymer hydrogels containing glucose oxidase, Polymer 41 (2000) 3975–3983.
[59] S. Brahim, D. Narinesingh, A. Guiseppi-Elie, Bio-smart hydrogels: co-joined molecular recognition and signal transduction in biosensor fabrication and drug delivery, Biosens. Bioelectron. 17 (2002) 973–981.
[60] G.P. Misra, E.S. Gil, T.L. Lowe, In the biomedical arena, Polymer Grafting and Crosslinking, Wiley, New York, 2009 145–175.
[61] J. Kopeček, J. Yang, Peptide-directed self-assembly of hydrogels, Acta Biomater. 5 (2009) 805–816.
[62] J. Kopeček, Smart and genetically engineered biomaterials and drug delivery systems, Eur. J. Pharm. Sci. 20 (2003) 1–16.
[63] R.V. Ulijn, N. Bibi, V. Jayawarna, P.D. Thornton, S.J. Todd, R.J. Mart, A.M. Smith, J.E. Gough, Bioresponsive hydrogels, Mater. Today 10 (2007) 40–48.
[64] T. Miyata, N. Asami, T. Uragami, A reversibly antigen-responsive hydrogel, Nature 399 (1999) 766–769.
[65] T. Miyata, T. Uragami, K. Nakamae, Biomolecule-sensitive hydrogels, Adv. Drug Deliv. Rev. 54 (2002) 79–98.
[66] T.G. Park, A.S. Hoffman, Immobilization of Arthrobacter simplex in a thermally reversible hydrogel: effect of temperature cycling on steroid conversion, Biotechnol. Bioeng. 35 (1990) 152–159.
[67] M. Suzuki, Amphoteric poly(vinyl alcohol) hydrogel as a material of artificial muscle, Kobunshi Ronbunshu 46 (1989) 603–611.
[68] J.L. Hill-West, S.M. Chowdhury, M.J. Slepian, J.A. Hubbell, Inhibition of thrombosis and intimal thickening by in situ photopolymerization of thin hydrogel barriers, Proc. Natl. Acad. Sci. 91 (1994) 5967–5971.
[69] A.J. DeFail, C.R. Chu, N. Izzo, K.G. Marra, Controlled release of bioactive TGF-β_1 from microspheres embedded within biodegradable hydrogels, Biomaterials 27 (2006) 1579–1585.
[70] H. Park, K. Park, Hydrogels in bioapplications, ACS Symposium Series, ACS Publications, New York, 1996 2–10.
[71] B. Jeong, A. Gutowska, Lessons from nature: stimuli-responsive polymers and their biomedical applications, Trends Biotechnol. 20 (2002) 305–311.
[72] P.H. Corkhill, C.J. Hamilton, B.J. Tighe, Synthetic hydrogels VI. Hydrogel composites as wound dressings and implant materials, Biomaterials 10 (1989) 3–10.

[73] A.R. Bontempo, J. Rapp, Protein–lipid interaction on the surface of a rigid gas-permeable contact lens in vitro, Curr. Eye Res. 16 (1997) 1258–1262.
[74] U. Darsow, D. Vieluf, J. Ring, Atopy patch test with different vehicles and allergen concentrations: an approach to standardization, J. Allergy Clin. Immunol. 95 (1995) 677–684.
[75] H. Abd El-Mohdy, A. Safrany, Preparation of fast response superabsorbent hydrogels by radiation polymerization and crosslinking of N-isopropylacrylamide in solution, Radiat. Phys. Chem. 77 (2008) 273–279.
[76] E. Vasheghani-Farahani, D.G. Cooper, J.H. Vera, M.E. Weber, Concentration of large biomolecules with hydrogels, Chem. Eng. Sci. 47 (1992) 31–40.
[77] M. Marchetti, E. Cussler, Hydrogels as ultrafiltration devices, Sep. Purif. Methods 18 (1989) 177–192.
[78] D.J. Overstreet, R.Y. McLemore, B.D. Doan, A. Farag, B.L. Vernon, Temperature-responsive graft copolymer hydrogels for controlled swelling and drug delivery, Soft Mater. 11 (2013) 294–304.
[79] X.-B. Yuan, Y.-B. Yuan, W. Jiang, J. Liu, E.-J. Tian, H.-M. Shun, D.-H. Huang, X.-Y. Yuan, H. Li, J. Sheng, Preparation of rapamycin-loaded chitosan/PLA nanoparticles for immunosuppression in corneal transplantation, Int. J. Pharm. 349 (2008) 241–248.
[80] M.J. Whitcombe, I. Chianella, L. Larcombe, S.A. Piletsky, J. Noble, R. Porter, A. Horgan, The rational development of molecularly imprinted polymer-based sensors for protein detection, Chem. Soc. Rev. 40 (2011) 1547–1571.
[81] C.-J. Kim, P.I. Lee, Composite poly(vinyl alcohol) beads for controlled drug delivery, Pharm. Res. 9 (1992) 10–16.
[82] T. Traitel, Y. Cohen, J. Kost, Characterization of glucose-sensitive insulin release systems in simulated in vivo conditions, Biomaterials 21 (2000) 1679–1687.
[83] R. Yoshida, K. Sakai, T. Okano, Y. Sakurai, Pulsatile drug delivery systems using hydrogels, Adv. Drug Deliv. Rev. 11 (1993) 85–108.
[84] N.A. Peppas, Hydrogels and drug delivery, Curr. Opin. Colloid Interface Sci. 2 (1997) 531–537.
[85] R.M.K. Ramanan, P. Chellamuthu, L. Tang, K.T. Nguyen, Development of a temperature-sensitive composite hydrogel for drug delivery applications, Biotechnol. Prog. 22 (2006) 118–125.
[86] A. Gutowska, Y.H. Bae, J. Feijen, S.W. Kim, Heparin release from thermosensitive hydrogels, J. Control. Release 22 (1992) 95–104.
[87] G. Crini, P.-M. Badot, Application of chitosan, a natural aminopolysaccharide, for dye removal from aqueous solutions by adsorption processes using batch studies: a review of recent literature, Prog. Polym. Sci. 33 (2008) 399–447.
[88] K.V. Kumar, K. Porkodi, Relation between some two-and three-parameter isotherm models for the sorption of methylene blue onto lemon peel, J. Hazard. Mater. 138 (2006) 633–635.
[89] M. Dalaran, S. Emik, G. Güçlü, T.B. İyim, S. Özgümüş, Study on a novel polyampholyte nanocomposite superabsorbent hydrogels: synthesis, characterization and investigation of removal of indigo carmine from aqueous solution, Desalination 279 (2011) 170–182.
[90] G.-B. Jiang, Z.-T. Lin, X.-Y. Huang, Y.-Q. Zheng, C.-C. Ren, C.-K. Huang, Z.-J. Huang, Potential biosorbent based on sugarcane bagasse modified with tetraethylene-pentamine for removal of eosin Y, Int. J. Biol. Macromol. 50 (2012) 707–712.
[91] G. Zhao, X. Wu, X. Tan, X. Wang, Sorption of heavy metal ions from aqueous solutions: a review, Open Colloid Sci. J. 4 (2011) 19–31.
[92] E. Guibal, Interactions of metal ions with chitosan-based sorbents: a review, Sep. Purif. Technol. 38 (2004) 43–74.
[93] G.S. Chauhan, S. Mahajan, Use of novel hydrogels based on modified cellulosics and methacrylamide for separation of metal ions from water systems, J. Appl. Polym. Sci. 86 (2002) 667–671.
[94] W. Wang, Y. Kang, A. Wang, One-step fabrication in aqueous solution of a granular alginate-based hydrogel for fast and efficient removal of heavy metal ions, J. Polym. Res. 20 (2013) 1–10.
[95] S. Zhao, F. Zhou, L. Li, M. Cao, D. Zuo, H. Liu, Removal of anionic dyes from aqueous solutions by adsorption of chitosan-based semi-IPN hydrogel composites, Compos. Part B 43 (2012) 1570–1578.
[96] Y. Zheng, Y. Zhu, A. Wang, Highly efficient and selective adsorption of malachite green onto granular composite hydrogel, Chem. Eng. J. 257 (2014) 66–73.
[97] Y.S. Jeon, J. Lei, J.-H. Kim, Dye adsorption characteristics of alginate/polyaspartate hydrogels, J. Ind. Eng. Chem. 14 (2008) 726–731.
[98] S. Li, Removal of crystal violet from aqueous solution by sorption into semi-interpenetrated networks hydrogels constituted of poly (acrylic acid-acrylamide-methacrylate) and amylose, Bioresour. Technol. 101 (2010) 2197–2202.
[99] A.M. Wilson, G. Justin, A. Guiseppi-Elie, Electroconductive hydrogels, Biomedical Applications of Hydrogels Handbook, Springer, 2010 319–337.
[100] Z. Yue, S.E. Moulton, M. Cook, S. O'Leary, G.G. Wallace, Controlled delivery for neuro-bionic devices, Adv. Drug Deliv. Rev. 65 (2013) 559–569.
[101] J.M. Fonner, L. Forciniti, H. Nguyen, J.D. Byrne, Y.-F. Kou, J. Syeda-Nawaz, C.E. Schmidt, Biocompatibility implications of polypyrrole synthesis techniques, Biomed. Mater. 3 (2008) 034124.
[102] T. Jamnongkan, S. Kaewpirom, Potassium release kinetics and water retention of controlled-release fertilizers based on chitosan hydrogels, J. Polym. Environ. 18 (2010) 413–421.
[103] H. Agaba, L.J. Orikiriza, J. Obua, J.D. Kabasa, M. Worbes, A. Hüttermann, Hydrogel amendment to sandy soil reduces irrigation frequency and improves the biomass of *Agrostis stolonifera*, Agric. Sci. 2 (2011) 544.
[104] C. Demitri, F. Scalera, M. Madaghiele, A. Sannino, A. Maffezzoli, Potential of cellulose-based superabsorbent hydrogels as water reservoir in agriculture, Int. J. Polym. Sci. 2013 (2013) 1–6.
[105] P.C. Parvathy, A. Jyothi, Rheological and thermal properties of saponified cassava starch-g-poly(acrylamide) superabsorbent polymers varying in grafting parameters and absorbency, J. Appl. Polym. Sci. 131 (2014) 1–11.
[106] E.V.R. Campos, J.L. de Oliveira, L.F. Fraceto, B. Singh, Polysaccharides as safer release systems for agrochemicals, Agron. Sustain. Dev. 35 (2015) 47–66.
[107] X. Zeng, H. Jiang, Liquid tunable microlenses based on MEMS techniques, J. Phys. D. Appl. Phys. 46 (2013) 323001.
[108] M. Jikei, M.-a. Kakimoto, Dendritic aromatic polyamides and polyimides, J. Polym. Sci. A Polym. Chem. 42 (2004) 1293–1309.
[109] G.R. Hendrickson, M.H. Smith, A.B. South, L.A. Lyon, Design of multiresponsive hydrogel particles and assemblies, Adv. Funct. Mater. 20 (2010) 1697–1712.
[110] G. Gorrasi, V. Bugatti, V. Vittoria, Pectins filled with LDH-antimicrobial molecules: preparation, characterization and physical properties, Carbohydr. Polym. 89 (2012) 132–137.
[111] C. Schmitt, S.L. Turgeon, Protein/polysaccharide complexes and coacervates in food systems, Adv. Colloid Interf. Sci. 167 (2011) 63–70.
[112] G. Scrinis, K. Lyons, Nanotechnology and the techno-corporate agri-food paradigm, Food Security, Nutrition and Sustainability2010 252–270 (DOI).
[113] C.M. Müller, J.B. Laurindo, F. Yamashita, Effect of cellulose fibers addition on the mechanical properties and water vapor barrier of starch-based films, Food Hydrocoll. 23 (2009) 1328–1333.
[114] M. Aider, Chitosan application for active bio-based films production and potential in the food industry: review, LWT—Food Sci. Technol. 43 (2010) 837–842.
[115] L. Wang, M.A. Auty, J.P. Kerry, Physical assessment of composite biodegradable films manufactured using whey protein isolate, gelatin and sodium alginate, J. Food Eng. 96 (2010) 199–207.
[116] J. Gómez-Estaca, A.L. de Lacey, M. López-Caballero, M. Gómez-Guillén, P. Montero, Biodegradable gelatin–chitosan films incorporated with essential oils as antimicrobial agents for fish preservation, Food Microbiol. 27 (2010) 889–896.
[117] M. Gómez-Guillén, B. Giménez, M.A. López-Caballero, M. Montero, Functional and bioactive properties of collagen and gelatin from alternative sources: a review, Food Hydrocoll. 25 (2011) 1813–1827.
[118] E.A. Baldwin, R. Hagenmaier, J. Bai, Edible Coatings and Films to Improve Food Quality, CRC Press, 2011.
[119] E. Leroy, P. Jacquet, G. Coativy, A. laure Reguerre, D. Lourdin, Compatibilization of starch–zein melt processed blends by an ionic liquid used as plasticizer, Carbohydr. Polym. 89 (2012) 955–963.
[120] S. Farris, K.M. Schaich, L. Liu, L. Piergiovanni, K.L. Yam, Development of polyion-complex hydrogels as an alternative approach for the production of bio-based polymers for food packaging applications: a review, Trends Food Sci. Technol. 20 (2009) 316–332.
[121] S. Cochran, T. Brockman, A cosmetic ingredient innovation for the stabilization and delivery of volatile fluoroether with cosmetic applications, J. Cosmet. Sci. 58 (2006) 413–419.
[122] V. Patravale, S. Mandawgade, Novel cosmetic delivery systems: an application update, Int. J. Cosmet. Sci. 30 (2008) 19–33.
[123] B. Bai, L. Li, Y. Liu, H. Liu, Z. Wang, C. You, Preformed particle gel for conformance control: factors affecting its properties and applications, SPE Reserv. Eval. Eng. 10 (2007) 415–422.
[124] P. Tongwa, R. Nygaard, B. Bai, Evaluation of a nanocomposite hydrogel for water shut-off in enhanced oil recovery applications: design, synthesis, and characterization, J. Appl. Polym. Sci. 128 (2013) 787–794.
[125] G. Cavallaro, A. Gianguzza, G. Lazzara, S. Milioto, D. Piazzese, Alginate gel beads filled with halloysite nanotubes, Appl. Clay Sci. 72 (2013) 132–137.
[126] M. Cascone, S. Maltinti, N. Barbani, M. Laus, Effect of chitosan and dextran on the properties of poly(vinyl alcohol) hydrogels, J. Mater. Sci. Mater. Med. 10 (1999) 431–435.
[127] E.-R. Kenawy, E.A. Kamoun, M.S. Mohy Eldin, M.A. El-Meligy, Physically crosslinked poly (vinyl alcohol)-hydroxyethyl starch blend hydrogel membranes: synthesis and characterization for biomedical applications, Arab. J. Chem. 7 (2014) 372–380.
[128] M.-H. Huang, M.-C. Yang, Evaluation of glucan/poly(vinyl alcohol) blend wound dressing using rat models, Int. J. Pharm. 346 (2008) 38–46.
[129] N.J. Einerson, K.R. Stevens, W.J. Kao, Synthesis and physicochemical analysis of gelatin-based hydrogels for drug carrier matrices, Biomaterials 24 (2003) 509–523.
[130] G. Qing, M. Li, L. Deng, Z. Lv, P. Ding, T. Sun, Smart drug release systems based on stimuli-responsive polymers, Mini Rev. Med. Chem. 13 (2013) 1369–1380.
[131] M.T. Razzak, D. Darwis, Irradiation of polyvinyl alcohol and polyvinyl pyrrolidone blended hydrogel for wound dressing, Radiat. Phys. Chem. 62 (2001) 107–113.
[132] M. Razzaghi-Kashani, H. Hasankhani, M. Kokabi, Improvement in physical and mechanical properties of butyl rubber with montmorillonite organo-clay, Iran. Polym. J. 16 (2007) 671.
[133] K. Shalumon, K. Anulekha, S.V. Nair, S. Nair, K. Chennazhi, R. Jayakumar, Sodium alginate/poly(vinyl alcohol)/nano ZnO composite nanofibers for antibacterial wound dressings, Int. J. Biol. Macromol. 49 (2011) 247–254.
[134] E.M. Ahmed, F.S. Aggor, A.M. Awad, A.T. El-Aref, An innovative method for preparation of nanometal hydroxide superabsorbent hydrogel, Carbohydr. Polym. 91 (2013) 693–698.
[135] A.K. Saxena, Synthetic biodegradable hydrogel (PleuraSeal) sealant for sealing of lung tissue after thoracoscopic resection, J. Thorac. Cardiovasc. Surg. 139 (2010) 496–497.
[136] R.P. Washington, O. Steinbock, Frontal polymerization synthesis of temperature-sensitive hydrogels, J. Am. Chem. Soc. 123 (2001) 7933–7934.
[137] M.B.H. Othman, H. Md Akil, S.Z. Md Rasib, A. Khan, Z. Ahmad, Thermal properties and kinetic investigation of chitosan-PMAA based dual-responsive hydrogels, Ind. Crop. Prod. 66 (2015) 178–187.
[138] M.J. Zohuriaan-Mehr, K. Kabiri, Superabsorbent polymer materials: a review, Iran. Polym. J. 17 (2008) 451.
[139] M. Othman, H. Akil, H. Osman, A. Khan, Z. Ahmad, Synthesis, characterisation and thermal properties of hyperbranched polyimide derived from melamine via

emulsion polymerisation, J. Therm. Anal. Calorim. (2015) 1–14, http://dx.doi.org/10.1007/s10973-015-4464-9.
[140] K.L. Beers, S. Boo, S.G. Gaynor, K. Matyjaszewski, Atom transfer radical polymerization of 2-hydroxyethyl methacrylate, Macromolecules 32 (1999) 5772–5776.
[141] P. Li, J. Zhang, A. Wang, A novel N-succinyl chitosan-graft-polyacrylamide/attapulgite composite hydrogel prepared through inverse suspension polymerization, Macromol. Mater. Eng. 292 (2007) 962–969.
[142] J.K. Oh, D.I. Lee, J.M. Park, Biopolymer-based microgels/nanogels for drug delivery applications, Prog. Polym. Sci. 34 (2009) 1261–1282.
[143] F.H. Rodrigues, C. Spagnol, A.G. Pereira, A.F. Martins, A.R. Fajardo, A.F. Rubira, E.C. Muniz, Superabsorbent hydrogel composites with a focus on hydrogels containing nanofibers or nanowhiskers of cellulose and chitin, J. Appl. Polym. Sci. 131 (2014) 1–13.
[144] M.R. Guilherme, F.A. Aouada, A.R. Fajardo, A.F. Martins, A.T. Paulino, M.F. Davi, A.F. Rubira, E.C. Muniz, Superabsorbent hydrogels based on polysaccharides for application in agriculture as soil conditioner and nutrient carrier: a review, Eur. Polym. J. (2015). http://dx.doi.org/10.1016/j.eurpolymj.2015.04.017 (in press).
[145] K. Park, J. Chen, H. Park, Hydrogel composites and superporous hydrogel composites having fast swelling, high mechanical strength, and superabsorbent properties, US6271278 B1, 2001.
[146] A.D. Mohammed, D.A. Young, H. Vosloo, Synthesis and study of superabsorbent properties of acryloylated starch ester grafted with acrylic acid, Starch-Starke 66 (2014) 393–399.