

Synthesis of Hydrogels by Modification of Natural Polysaccharides Through Radiation Cross-Linking Polymerization for Use in Drug Delivery



Kashma Sharma, Vishal Sharma and Vijay Kumar

Abstract Hydrogels are three-dimensional polymer structures that can captivate and hold a vast quantity of water. They have superior's properties such as hydrophilicity, high swelling ability, non-toxic in nature, and biocompatibility which makes them prospective materials for various applications. The concept of graft copolymers in biomedical field developed in the past few ten years and lasts to fascinate researchers working in this sector. Research in this sector is ongoing with the aim of alteration of the inherent properties of polysaccharides after grafting, which offers premises to be pervasive in integrated systems with multiple functionalities or the enhanced properties of one domain. This chapter aims to give comprehensive details about research that have been made on radiation-induced synthesis of polysaccharide-based hydrogels in context to biomedical application. This review also intends to explain the mechanism of radiation-induced synthesis of hydrogels. The effect of various radiation sources such as gamma, microwave, electron, and heavy ions is also discussed. Also, current status and plans of hydrogels are presented along with proper citations extracted from the scientific literature. Moreover, this article provides you with essential information that one's need to start work in this area.

Keywords Polysaccharides · Hydrogels · Radiation · Cross-linking
Biomedical

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1 Historical Background

A polymer gel is defined as a solvent-comprising system in which sufficient numbers of cross-link present to tie all polymer chains to other chains at various points [1, 2]. It is considered as a unique state of matter because the polymer gel has solid- and liquid-like characteristics. The gels can be cross-linked either chemically or physically which leads to the construction of a bulky three-dimensional network soaking through the entire solution volume. The cross-linked gel networks are potentially very useful in many sectors such as pharmaceuticals, biotechnology, agriculture, food processing, and electronics [2].

The first scientific study of gels was carried out by Thomas Graham, who is also known as Father of Physical Chemistry in the nineteenth century [3]. He employed solgel chemistry in his work to yield a silica gel. The conventional chemical approach normally uses colloidal suspension followed by the removal of the solvent during synthesis of fine particulate solids. Solgel chemistry generally involves the preparation of concentrated solution of a metal salt in a dilute acid. During the synthesis process, pH of the solution was adjusted followed by the addition of a gelling material, finally vaporizing the liquid to yield a gel and heating the gel at a particular temperature to get fine particles of the material [3].

The 1940s and 1950s evidenced the growths of gels which is carried out by pioneers such as Flory [4, 5], Huggins [6, 7], and Treloar [8, 9]. Treloar is generally famous for his work in the investigation of elasticity in polymer structures. Paul Flory discovered the modern polymer science via using the experimental and theoretical investigations of macromolecules; for the same, he received the Nobel Prize in the year 1974 [10]. Currently, much interest and activity exist in synthesis, characterization, and applications of synthetic and natural polymers, mainly hydrogels for biomedical applications.

2 Hydrogels

Hydrogels are polymeric candidates which have the ability to regain a large measure of water owing to the presence of various hydrophilic groups, without dissolving in water, as there is cross-linking which helps to bind the various chains together [11, 12]. As soon as they come in closer with aqueous solutions or fluids, they swell up to a best level, which resembles to state about the osmotic pressure that pushes water inside the network and the retroactive elastic strength which comes from the strained hydrogel chains between the cross-links on swelling. The presence of water in hydrogels performs a crucial part in the complete penetration of active elements into and out of the gel. Water can be linked to any hydrogel network in subsequent techniques as displayed in Fig. 1.

The overall characteristics of the hydrogels are mainly dependent on various factors, viz. the hydrophilicity of the polymer chains and the magnitude of

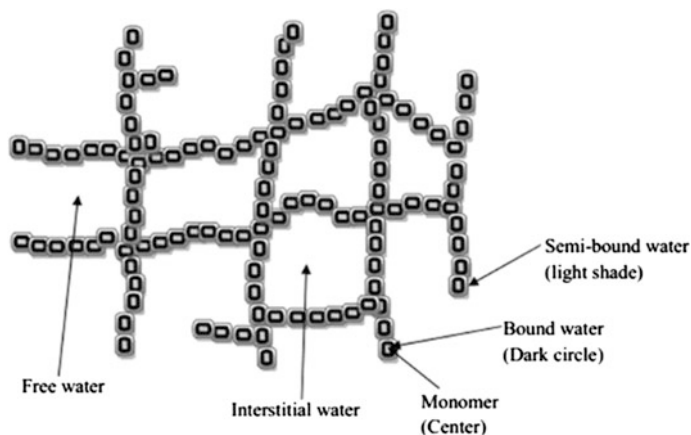


Fig. 1 Graphical representation of molecular structure of hydrogel network with different types of water [12]

cross-linking [12–16]. The water absorbing ability of the hydrogels linked with availability hydrophilic groups (such as $-\text{OH}$, $-\text{COOH}$, $-\text{CONH}-$, $-\text{CONH}_2$, and $-\text{SO}_3\text{H}$) in the polymer chains [2, 15–20]. Hydrogels have gained much responsiveness in the past thirty years, due to their remarkable potential in biomaterial fields [19]. The presence of a large number of water in the hydrogel occupies the voids and permits a particular circulation of solute molecules through the matrix. This behavior makes them better candidates to be used in a membrane separation process [21]. The formation of hydrogels can be done with various natural and synthetic backbones, which have extensive features and as a result found important applications in biomedical fields [15, 22, 23]. Hydrogels have existed in nature since the start of life. A variety of naturally occurring polymers such as collagen, alginate, agarose, and gelatin were also explored in early civilization [2]. The application of hydrogels in the medical field has been started in the year 1950s. The foremost synthetic hydrogel poly(2-hydroxyethyl methacrylate) has been prepared by DuPont’s scientists in 1936 [24].

Wichterle and Lim established the importance of poly(2-hydroxyethyl methacrylate) hydrogels as superb candidates for contact lens industry [25]. This development was the milestone in the contact lens business and to the novel field of biomedical hydrogels. Hydrogels undergo physiochemical changes in response to small variations in the experimental conditions such as temperature, pH, electric or magnetic field, enzymes, and solvent polarity, and such candidates are known as “smart hydrogels” [2, 26–30]. Previous research clearly indicates that hydrogels could be used in various research fields such as biomedical, agriculture, pharmaceuticals, and biotechnology [26–36]. Biopolymer-based cross-linked networks have become an interesting field of research in the sector of tissue engineering and regenerative medicine, owing to their extraordinary swelling behavior, mechanical resemblance to natural tissues, and simplicity of surgical grafting [37].

3 Classifications of Hydrogels

Based on the source of origin, synthesis method, ionic charge, or structural characteristics, hydrogel can be divided into various classes [2, 15, 38]. An organization of hydrogels based on their source is presented in Fig. 2.

On the Basis of Polymeric Composition: The synthesis process results in the construction of four types of hydrogels which may be:

Homopolymeric Hydrogels: are denoted to polymer chains imitative from only one kind hydrophilic monomer component [39]. Homopolymers can be cross-linked in very thin arrangement subject to the type of the monomer unit and the synthesis process.

Copolymeric Hydrogels: They are comprised of two or more monomer units; in any case, one of them should be hydrophilic to make them water swellable [40].

Multipolymer Hydrogels: They are synthesized from three or more than three monomers mixing together.

Interpenetrating Polymeric Hydrogel (IPN): IPNs were pronounced for the first time in the year 1914, once Aylsworth fabricated the first synthetic IPN for the application of gramophone record [41]. The researchers began to express their interest in IPNs after 1950s. The name “interpenetrating polymer network” was exactly introduced by Millar in the year 1960 [42]. Subsequently, lots of researches have been devoted to the preparation and characterization of IPNs for various uses by employing both synthetic and natural polymers [43–45]. A combination of two or more preformed polymer structures is not considered as IPN [46].

Classification Based on Type of Cross-Linking

Chemical hydrogels are normally synthesized via two dissimilar means: “three-dimensional polymerization” (Fig. 3), wherein a hydrophilic monomer combines to form a polymer in the vicinity of a multifunctional cross-linking mediator (Fig. 4) [22].

4 Synthesis of Hydrogels

Graft copolymerization is a generally employed technique for the surface treatment of polymeric backbones, and it is an important means to transform the physio-chemical features of backbones [47–50]. The pictorial representation of the polymer modification is shown in Fig. 5. The free radicals are formed on the backbone for the fabrication of graft copolymers during the process of polymerization [51]. Up to now, ample of synthesis techniques have been adopted for the production of active sites on the backbone and are generally classified as physical techniques, chemical approaches, photo-initiated grafting, plasma, radiation-induced grafting, enzymatic grafting, etc. Among them, chemical methods and radiation-induced graft copolymerization are extensively studied methods. There are large numbers of original

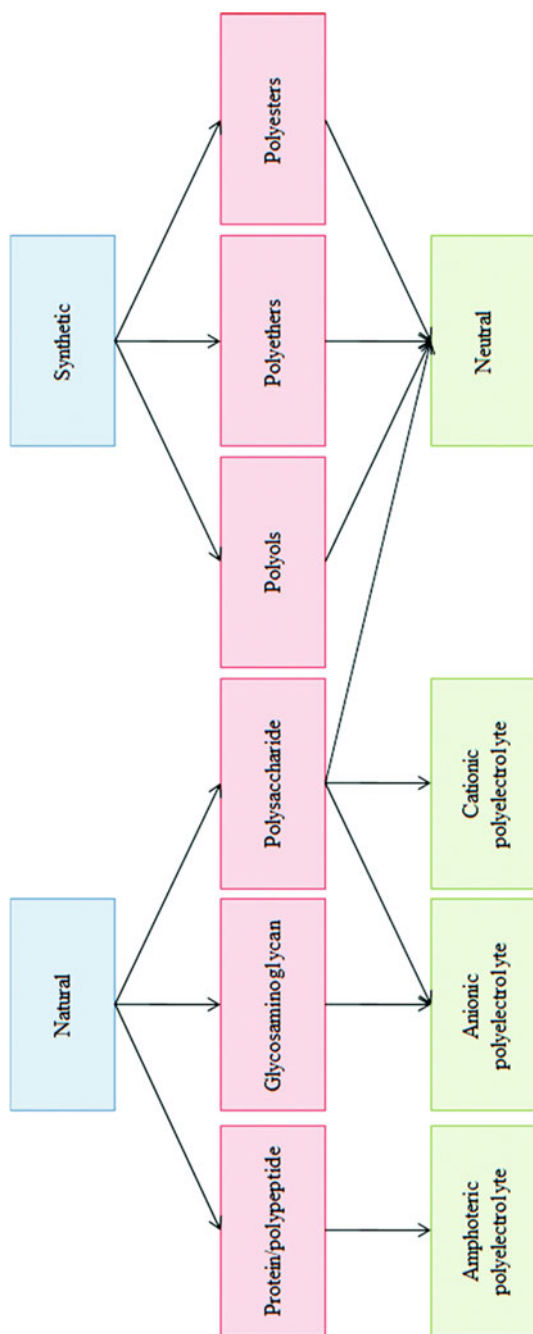


Fig. 2 Organization of hydrogels based on their source. Copied from Ref. [38] with consent from the Royal Society of Chemistry

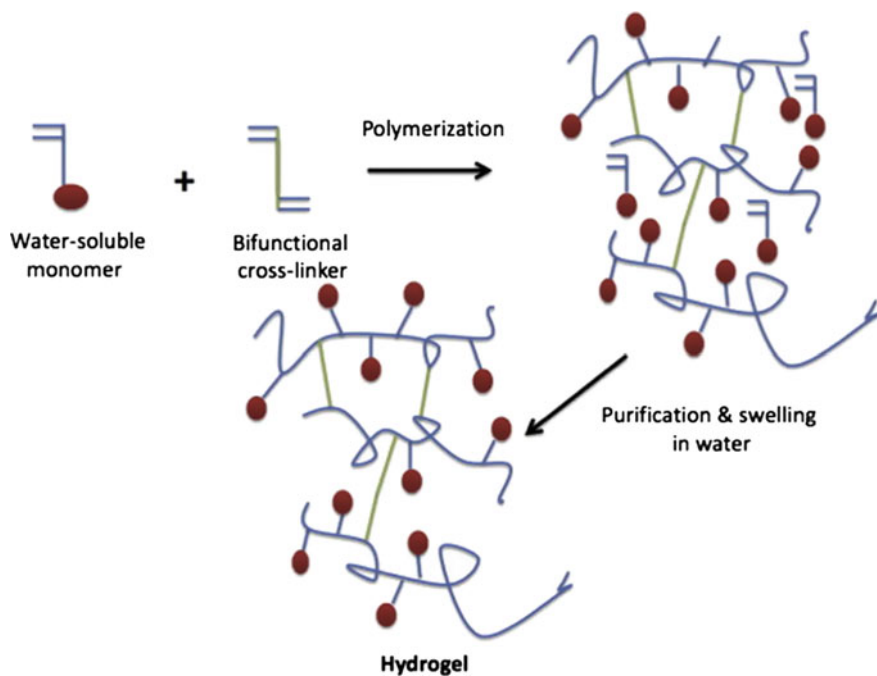


Fig. 3 Synthesis of hydrogels by three-dimensional polymerization [22]

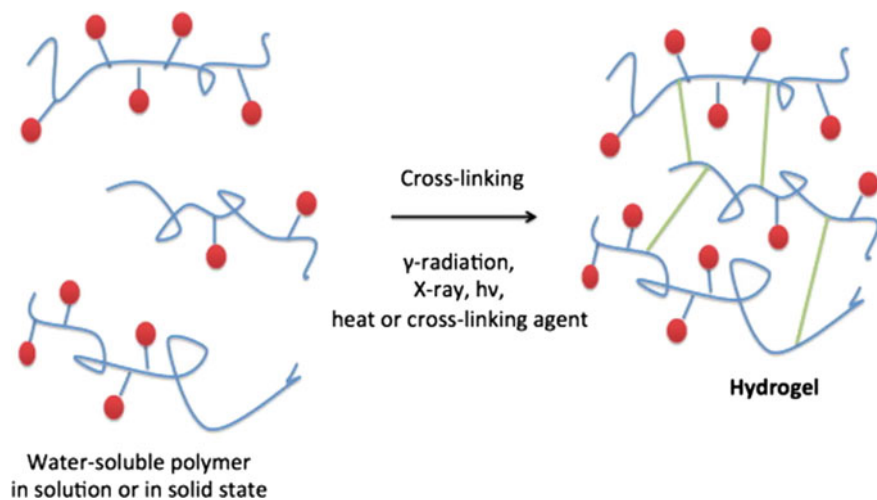


Fig. 4 Synthesis of hydrogels by cross-linking of readymade water-soluble polymers [22]

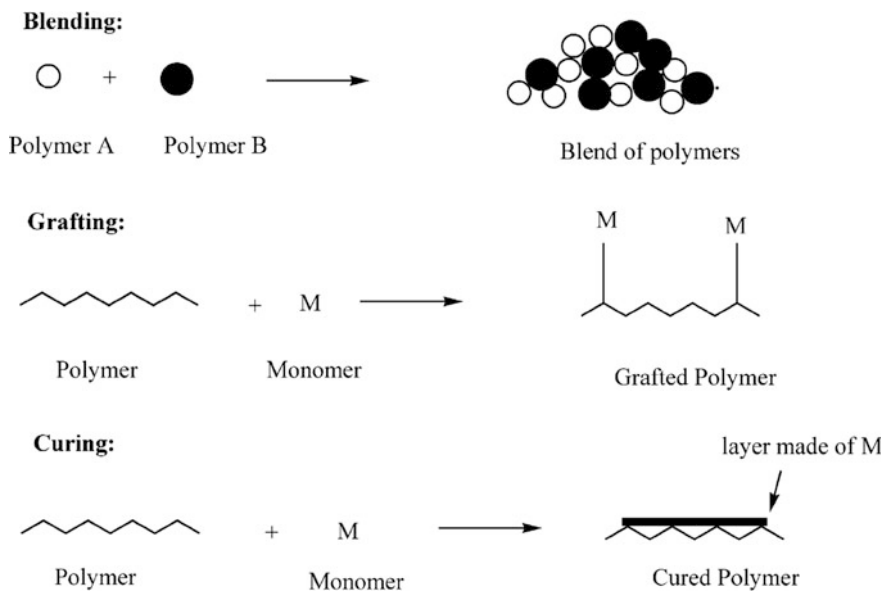


Fig. 5 Schematic representation of the methods of polymer modification. Copied from Ref. [47] with consent from the Elsevier

research papers and detailed review articles concentrated on the fabrication, properties, and applications of hydrogels. This chapter gives a detailed literature for the synthesis of hydrogels through radiation cross-linking and their applications in numerous biomedical sectors.

4.1 Chemical Synthesis of Hydrogels

Various initiators, viz. conventional radical initiators, ammonium persulfate (APS), ceric ammonium nitrate (CAN), potassium persulfate (KPS), potassium permanganate (KMnO_4), have been successfully used for the chemical grafting [2, 52–54]. Various authors grafted a wide variety of monomers onto natural polysaccharides by use of radical initiator [55–57]. In the case of chemical synthesis, active sites are generated from the initiators and shifted to the backbone to act in response to monomer to form the graft copolymers [47]. The part of the initiator is essential as it decides the route of the grafting process. A variety of cross-linked hydrogels have been synthesized by chemical synthesis method [58]. In general, free radical polymerization has four kinds of reactions [2, 59]:

- i. Production of active species (initiation)
- ii. Addition of these active species to a substituted alkene (propagation)
- iii. Atom transfer and atom abstraction reactions (chain transfer and termination by disproportionately)
- iv. Radical–radical recombination reactions (termination by coupling).

4.2 Radiation-Induced Synthesis of Hydrogels

Radiation-induced grafting is the more favorable technique for the graft copolymerization. When electromagnetic radiations go through the material, it leads in the creation of free radicals for the reaction (Fig. 6). There are many advantages of the synthesis of hydrogels by radiation processing such as ionizing radiation, gamma (γ) radiations, or electron beam over the conventional methods [60]. In the event of radiation-induced synthesis, the chemical reactions in the matrices are instigated by radiation, and there is no requirement to use (usually toxic) initiators, cross-linking agents, or other secondary materials [60–68]. This supports to cut prices, makes the technology easy, does not lead to secondary products, and the resultant material is of high purity.

Grafting can initiate either in the presence of low or high energy radiations [47]. Bombardment of polymer matrix with low energy radiations like ultraviolet and visible light leads in the homolytic splitting to created active sites on the backbone [47]. Under the influence of low energy radiations, polymerization can be initiated with or without photo-initiator. Possible biomedical applications of hydrogels have been found in implants, topical dressings, and drug delivery devices. As a result, radiation-induced cross-linking of polymers is considered important for medical applications, where even a pinch of small impurity is unwanted. A tremendous amount of work has been carried out on radiation-induced synthesis of natural polymers, and the realization of various applications has been achieved. The focus on natural polymers is due to their distinctive characteristics like intrinsic biocompatibility, biodegradability, and easy accessibility. Usually, the marketable use of natural polymers, like gum ghatti, carrageenans, alginates, starch, and cellulose, has been based mainly on existing knowledge.

The progress in the field of radiation-induced synthesis of hydrogels for various applications has been started in the late 1960s as reported by various researchers

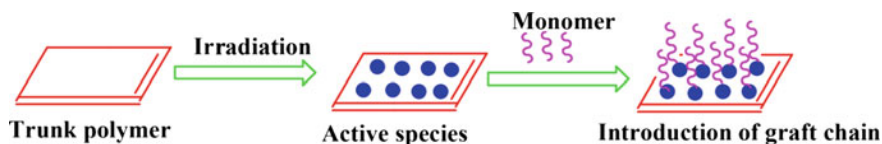


Fig. 6 Schematic representation of “radiation-induced grafting”

[69–71]. The much work in this direction has been carried out by Rosiak and coworkers by understanding the fundamental of radiation physics and chemistry as well as popularize the growth of an industrial products out of them [72, 73]. The ease of the radiation process, the prospect of uniting sterilization and cross-linking in a real-time process, and the backing of the International Atomic Energy Agency (IAEA) in endorsing the technology transfer of the radiation-induced synthesis of hydrogels by various researchers all across the globe and at a same time promoting the use of this technology in other countries [74]. Radiation has been extensively applied with the purpose of inducing cross-linking in polymeric materials [75–77].

4.2.1 Gamma Radiation-Induced Synthesis of Natural Gum-Based Hydrogels

Gamma radiations are the ionizing radiations and useful for the preparation and modification of materials for biomedical uses. It also offers unique advantages like easy process control, sterilization, high impurity, zero cross-linking agents, and fewer waste products [74]. Solpan and co-worker prepared acrylamide- and acrylic acid-based hydrogels in the cylindrical form by gamma-induced irradiation method involving 2.6–20.0 kGy rays [78]. Alam and coworkers reported that hydrogels have been prepared in from 10, 20, 30, 40, 50, and 60% aqueous solutions of acrylamide monomer by gamma radiation using gamma doses varied from 0.2 to 30 kGy [79]. A group of researchers from Gazi University, Besevler, Ankara, prepared macroporous poly(acrylamide) [poly(AAm)] hydrogels by using poly(ethylene glycol) (PEG) by using gamma radiation-induced grafting [80]. Our group has carried out γ -irradiation-induced grafting of various vinyl monomers and aniline onto gum ghatti [34, 35, 81]. The possible mechanism of γ -irradiation-induced synthesis of acrylic acid grafted onto gum ghatti is depicted in Fig. 7. The synthesized hydrogels are successfully used for the elimination of methylene orange from wastewater. In addition, these candidates can be employed as ion exchangers to enhance their efficacy for dye removal wastewater [35]. The addition of water-hating groups into these hydrogels makes them better candidates to control the oil spill in the oceans. The synthesized hydrogels based on gum ghatti (Gg)/methacrylic acid (MAA)/aniline (ANI) can be employed in the construction of site-specific drug delivery devices where rapid release of the drug is preferred in the beginning and constant release afterward [34].

The researchers varied the different reaction conditions to get the product with optimum percentage swelling. Seo and coworkers synthesized cross-linked PVA-gelative copolymers in the presence of γ -ray irradiations [82]. They have reported that the synthesized hydrogel candidate revealed promising physical properties, which is necessary for the construction of diploid cell culture. Taleb et al. [83] performed γ -ray-induced cross-linking and synthesis PVA and methacrylic acid (MAAc) onto gelatin, which leads to the formation of PVA/MAAc/gelatin copolymer [83]. The synthesize hydrogels can be employed for antibiotic drug carrier and as encouraging candidate for wound-healing

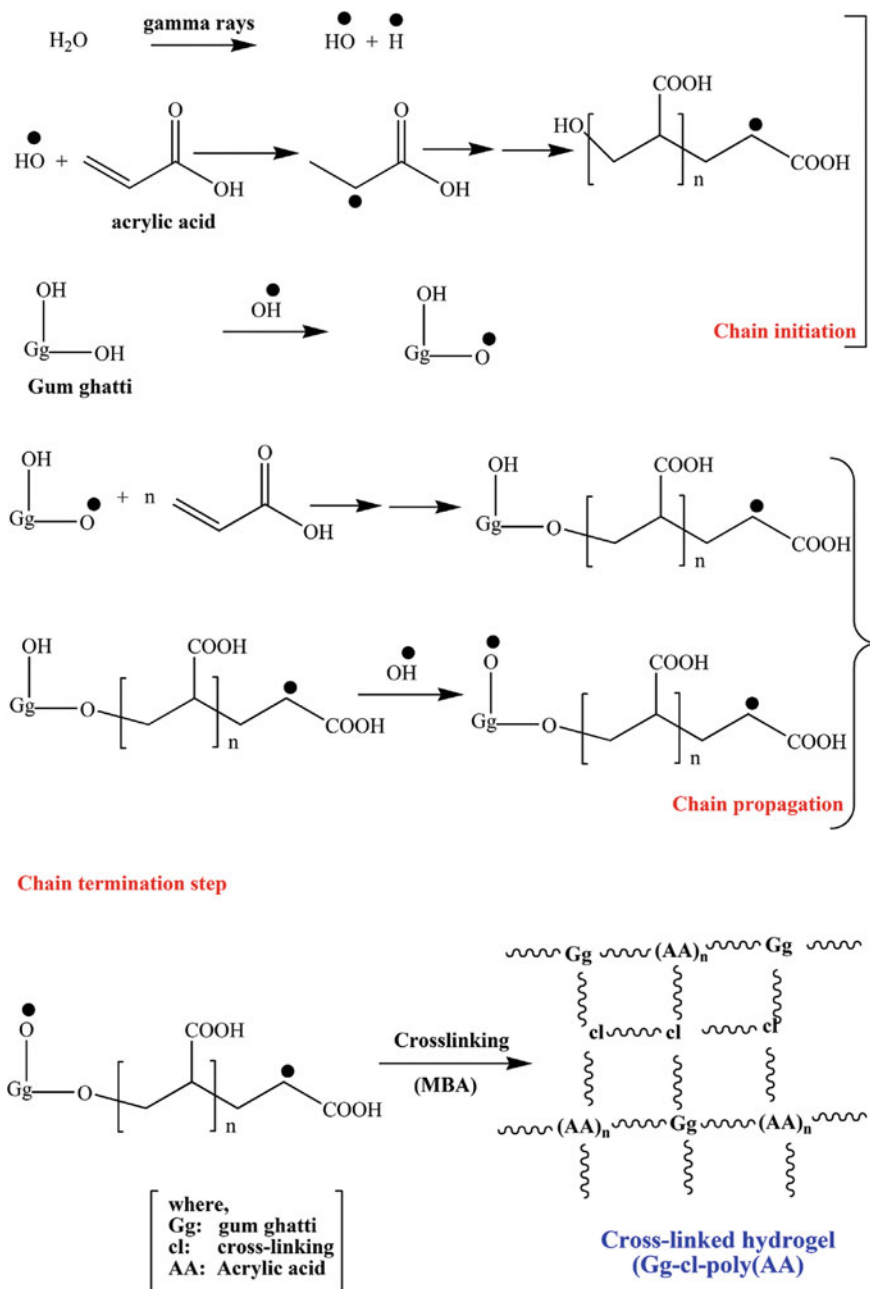


Fig. 7 Mechanism of graft copolymerization of acrylic acid onto gum ghatti [35]

applications. Synthesis and characterization of novel graft copolymers based on N-vinyl-2-pyrrolidone (NVP), 4-vinyl pyridine (4VP), and 2-vinyl pyridine (2VP) monomers onto poly(ethylene-alt-tetrafluoroethylene) (ETFE) by radiation-induced grafting have been reported [84]. It is well reported in the literature that the extent of grafting is directly related to various factors, viz. kind of polymer and monomer, monomer concentration, type of radiation, temperature, reaction atmosphere, concentration of homopolymerization suppressor, and type of solvent [85–87]. As a result, the effectiveness of the method can be managed by the optimization of these reaction parameters. Hamzah and coworkers carried out gamma radiation-induced synthesis of nanocurcumin and studied cell viability [88]. They have concluded that the use of radiation technique is a pretty easy and clean approach of fabricating nanocurcumin. Recently, Fekete et al. performed gamma irradiation-induced synthesis of carboxymethylcellulose/starch superabsorbent hydrogels [89]. They have studied the effect of absorbed dose on the percentage swelling. Mahmoud et al. (2014) carried out a gamma radiation-induced synthesis of hydrogels based on starch, acrylic acid, and 2-hydroxyethyl methacrylate, and the synthesized hydrogels have been used for the removal of red dye from aqueous solution [90]. Varshney et al. (2007) have synthesized polyvinyl alcohol, carrageenan, and agar-based hydrogel film via gamma irradiation which was elastic even without plasticizer and was mechanically tough and biocompatible [91]. Singh and coworkers have fabricated tragacanth gum-based sterile hydrogel films via gamma radiation and their utilization in drug delivery devices [92]. The hydrogels films were made by changing the gamma radiation from 9.1 to 63.5 kGy and evaluated their swelling capacity (Fig. 8). The synthesized hydrogels are also suitable materials to be used in wound dressings owing to their sterile and biocompatible nature. In another study, Singh and coworkers have synthesized tragacanth gum-based hydrogels films by gamma radiation for wound-dressing application [93]. The formation of tragacanth gum-cl-PVA-co-PVP-based hydrogel by means of gamma radiation is schematically shown in Fig. 9. Preparation, characterization, and swelling behavior of gamma-induced synthesized guar gum-based pH, temperature, and salt-responsive hydrogels have been carried out by Dharela and coworkers [94], whereas Co60 γ radiation-induced synthesis of acrylamide-grafted guar gum-based hydrogels has been reported by Biswal and coworkers [95]. They have also studied the flocculating properties of the synthesized hydrogels for industrial effluents.

4.2.2 Microwave-Assisted Synthesis of Gum-Based Hydrogels

Microwave radiation is the alternative source of energy and is evolving as an important means for the preparation of a variety of graft copolymers. Microwave-assisted technique reveals the finest prospective for preparing hydrogels, for the reason that the active species are created by the use of microwave radiation along with free radical initiators, exhibiting a better percentage of grafting in comparison with the other methods [96–100]. Microwave heating is totally

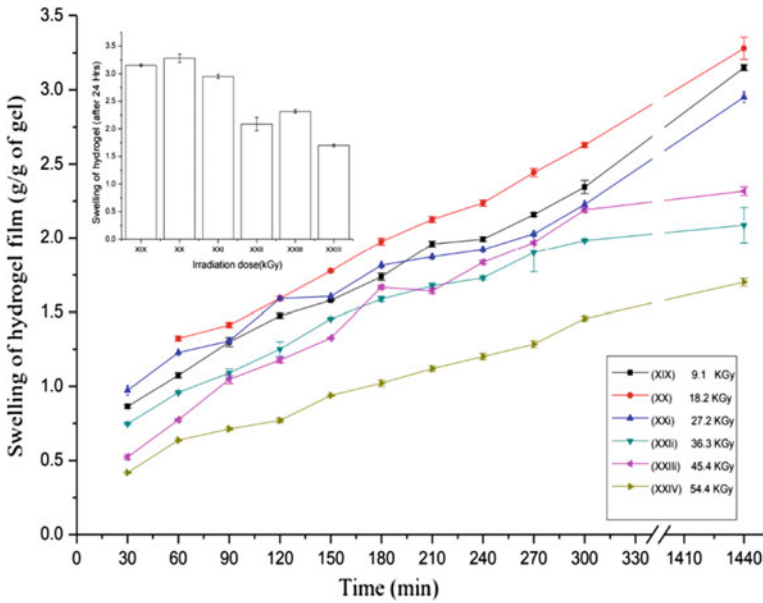


Fig. 8 Influence of gamma radiation dose on swelling capacity of TG-co-SA-cl-PVA polymer films in distilled water at 37 °C. Inset figure shows the effect of irradiation dose on swelling of hydrogel film after 24 h. Reproduced with permission from Ref. [92] from the Elsevier

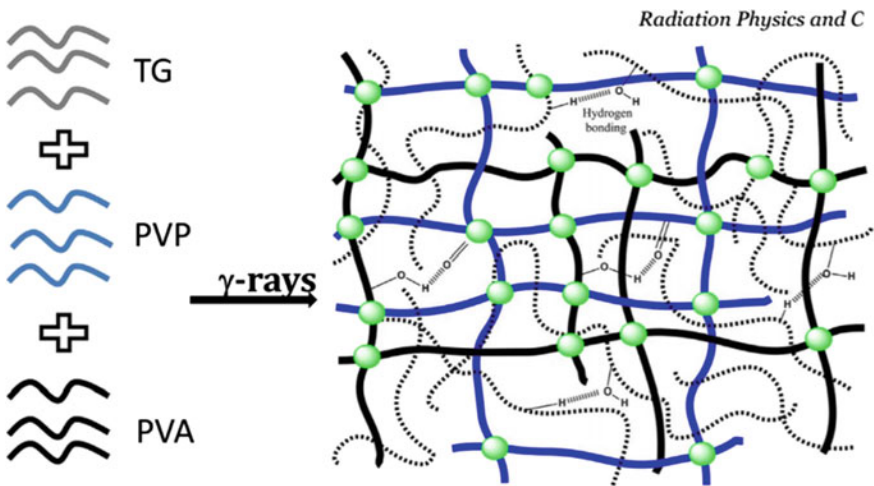


Fig. 9 Formation mechanism of tragacanth gum-cl-PVA-co-PVP-based hydrogel by means of gamma radiation. Reproduced with permission from Ref. [93] from the Elsevier

different from various other existing heating techniques. In microwave heating, heat is produced within the matrix but not created from any outerheating source [36, 101]. It has various other benefits, which comprise green synthesis, no secondary product, quick reaction speed, and capability of form nanostructures (Fig. 10).

We have conducted microwave-assisted grafting of vinyl monomers onto polysaccharide gum ghatti [32, 36, 102]. General scheme for the grafting of gum ghatti with vinyl monomers is presented in Fig. 11. Reactive chains for grafting of vinyl monomers onto polysaccharide gum ghatti are the $-OH$ and $-CH$ groups. Ammonium persulfate (APS) is a thermal initiator and gets dissociated under microwave irradiation leading to the creation of sulfate ion radicals. $SO_4^{\cdot-}$ on reaction with water molecules gives rise to the formation of OH^{\cdot} and HSO_4^- . OH^{\cdot} free radicals and $SO_4^{\cdot-}$ both generate active sites on backbone and monomer

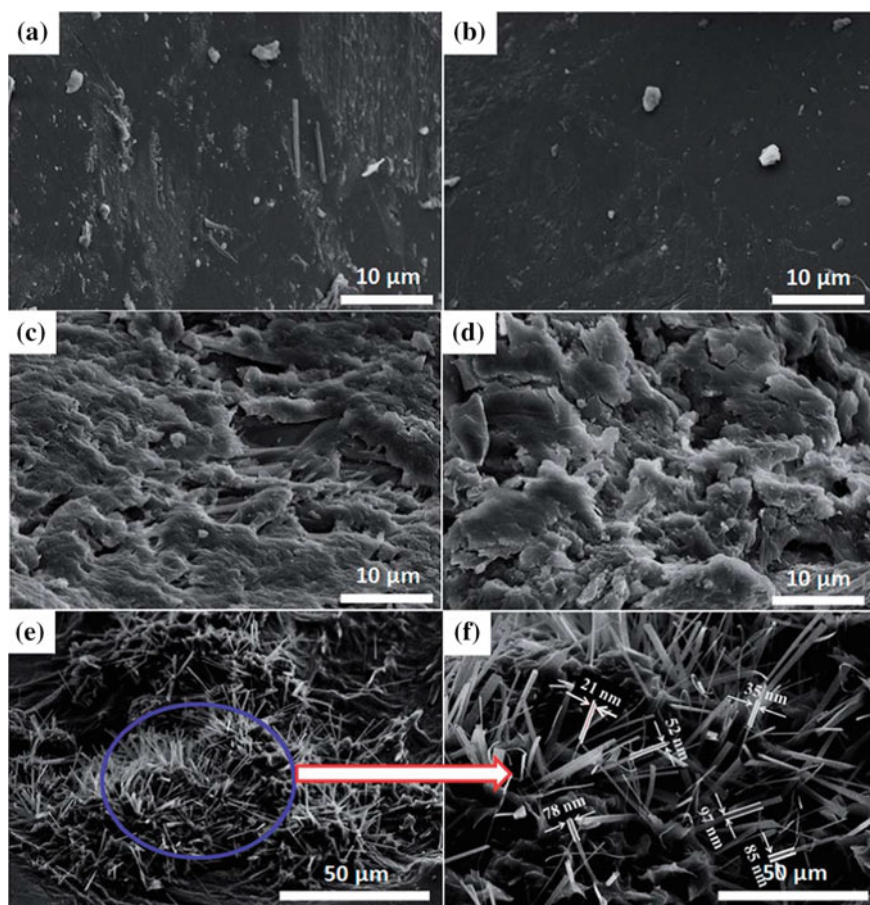


Fig. 10 SEM micrographs of **a, b** gum ghatti, **c, d** Gg-cl-poly(AAm), and **e, f** Gg-cl-poly(AAm-ipn-aniline) [36]

graft copolymers. MBA undergoes cross-linking between the various poly(vinyl) chains, in this manner leading to the formation of semi-IPNs [32, 36, 98–103].

Various authors have carried out microwave supported synthesis of hydrogels based on numerous synthetic and natural polymers [104–117]. A comprehensive review article stressed the various applications of microwave-induced synthesis of polysaccharides-based hydrogels and also covered the fundamental mechanism, and related problems were reviewed by Singh and coworkers [118]. This review article covered the microwave induced synthesis of various polysaccharides such as gum acacia, alginate, artemisia seed gum, cellulose, fibers, chitin and chitosan, guar gum, cassia seed gums, starch, konjac glucomannan, carboxymethyl starch, agar and carrageenan, and xanthan gum. Graphical representation of microwave-assisted grafting of the polysaccharides is displayed in Fig. 12.

4.2.3 Electron Radiation-Induced Synthesis of Hydrogels

As mentioned earlier that many of techniques have been employed for the synthesis hydrogels [119–122], It is also stated that the beginning of chemical reactions by the means of radiation is gradually employed for the synthesis of new hydrogel candidates. The radiation-induced synthesis technique is better than the chemical one, because of the benefit presented by the control of the amount of cross-linking

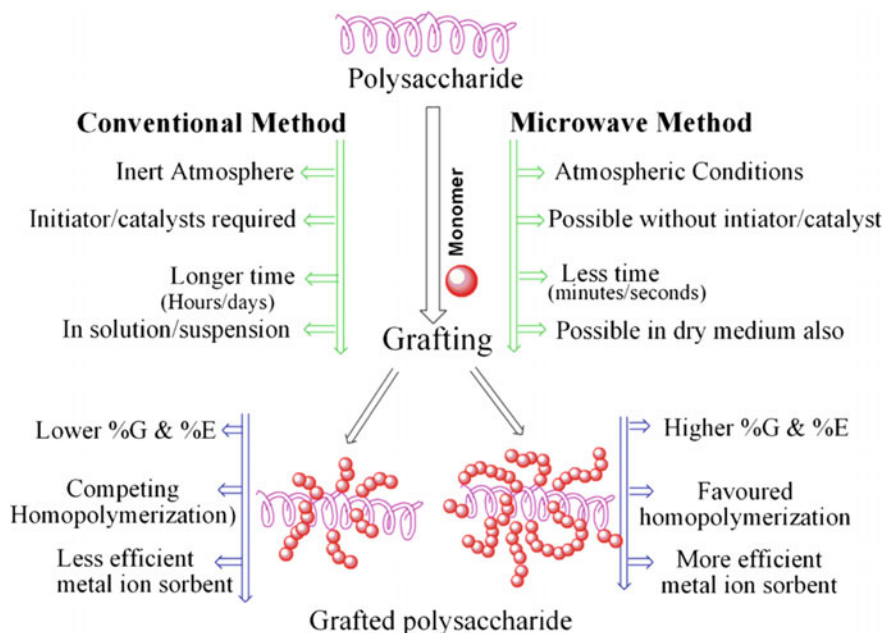


Fig. 12 Schematic diagram of microwave-assisted grafting of the polysaccharides. Reproduced with permission from Ref. [118] from the Elsevier

by simply varying the time of irradiation, which is related to the absorbed dose [119]. It is easy without any chemical initiation which is taking place at any temperature; the reactions such as polymerization, cross-linking, and grafting can be certainly adjusted, and the exposure can be restricted to a definite region [123]. Electron beam-induced synthesis of nanostructure has been recently reviewed by Gonzalez-Martinez and coworkers [124]. The processing of materials by irradiation with fast-moving electrons eliminates many shortcomings of the chemical methodologies, since ionizing radiation starts polymerization devoid of external thermal energy, owing to free radicals that are generated at the interaction with the monomers and with the solvent. Therefore, a better option to synthesize hydrogel networks is to employ ionizing radiation and particularly electron beams, which direct their energy in the volume of the polymeric matrix to be irradiated [125–127]. The impacts of electron irradiation on the structure, the conformation and the optical and mechanical properties of polymers have been extensively investigated in the literature [128–135].

4.2.4 Heavy Ion-Induced Modifications and Synthesis of Hydrogels

It is also widely accepted that polymers undergo structural alterations due to the impact of heavy ion irradiation [136, 137]. Irradiation of polymers induced the generation of highly reactive species, cross-linking, and oxidative breakage of bonds [138]. The supremacy of the above processes is evaluated by various factors like polymer structure and irradiation conditions (such as the atmosphere, LET, radiation dose, dose rate, sample thickness, and irradiation temperature). These changes have a direct association with the macroscopic properties for the target materials [136–138]. Although, a significant amount of work has already been done over the synthesis and characterizations of hydrogels by irradiation. But there are very few reports on the structural and morphological properties of cross-linked hydrogels after irradiation [139–142]. In our first report, we have investigated the effects of 100 meV O^{7+} ions irradiation on the structural and morphological behavior of poly(methacrylic acid)-cross-linked gum ghatti films [140]. Subsequently, a comparative study has been reported to study the influence of Ni^{9+} and Au^{8+} ions beam on the various properties of poly(methacrylic acid)-cross-linked gum ghatti films [141]. From these studies, we have concluded that there was a noticeable decrease in transmittance values which was ascribed to chain scissioning and cross-linking of the polymer chains. The overall surface morphologies of the irradiated hydrogel films got modified after irradiation. In another study, we have reported the effects of O^{7+} and Ni^{9+} heavy ions irradiation on polyacrylamide-grafted gum acacia thin films and sorption of methylene blue [142]. The sorption trend of pure and irradiated hydrogel films with O^{7+} and Ni^{7+} ions at a fluence of 1×10^{12} ions/cm² as a function of time has been studied separately (Fig. 13). The so-induced changes have been discussed by taking into account the linear energy transfer of these ions. The influences of irradiation on controlled drug

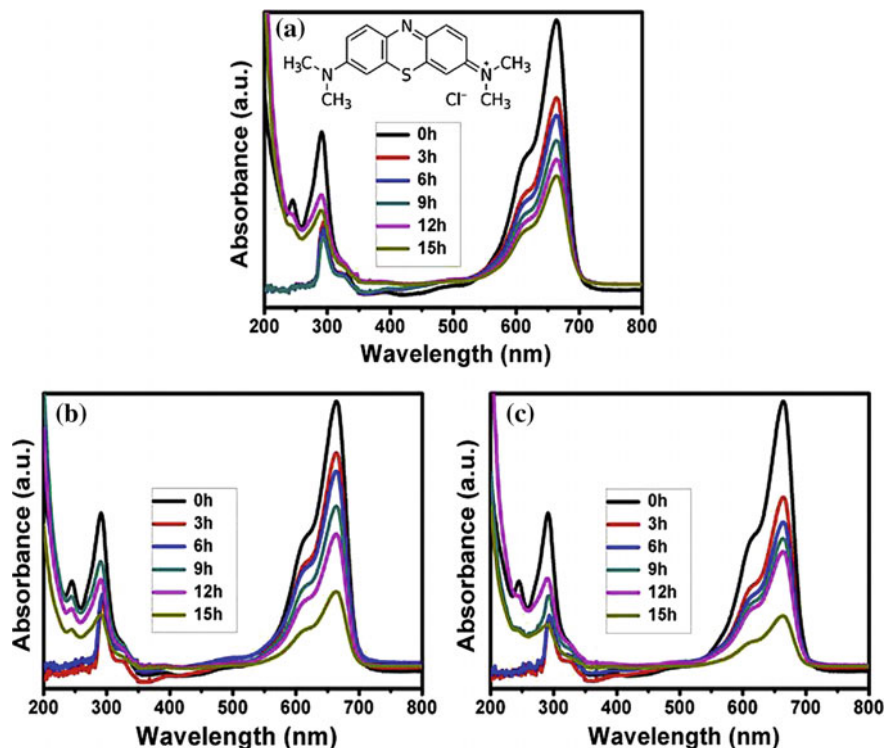


Fig. 13 UV-visible spectra of MB dye solution kept in contact with cross-linked hydrogel thin film, **a** pristine, **b** O^{7+} ion irradiated at fluence 1×10^{12} ions/cm², and **c** Ni^{9+} ion irradiated at fluence 1×10^{12} ions/cm²

delivery devices have been studied by various authors and reported that ion-beam irradiation is a very important tool for modifying the surface properties of polymeric materials without losing the bulk properties [143–145].

5 Miscellaneous

Ultraviolet radiation-initiated synthesis of methyl acrylate onto the sodium salt of partially carboxymethylated guar gum has been carried by researchers [146]. A group of researchers from Koc University, Istanbul, Turkey, reported a new process for the preparation of a pH-sensitive composite hydrogel using visible light [147]. They have used the synthesized composite hydrogel for controlled drug delivery of the anticonvulsant drug pregabalin. Further, they have conducted in vitro human fibroblast survival assay and in vivo rabbit grafting tests and

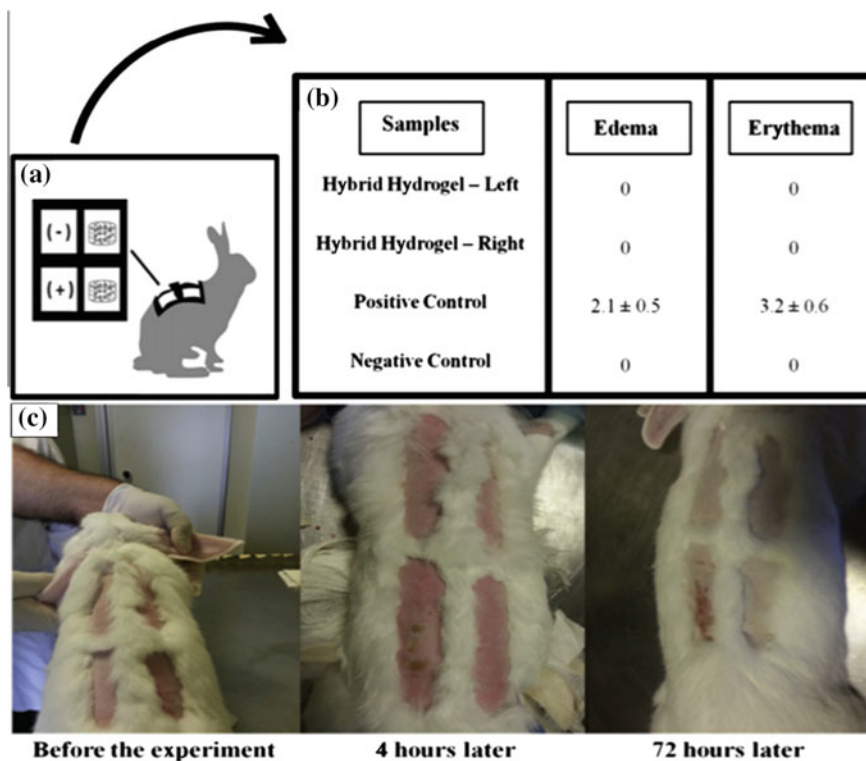


Fig. 14 In vivo implantation experiment results for an irritation assay. **a** Schematic representation of intracutaneous reactivity assay sites, **b** results of intracutaneous reaction, and **c** photographic images of implantation experiments before the experiment, 4 h later, and 72 h later. Reproduced with permission from Ref. [147] from the Elsevier

confirmed that the composite hydrogel is not toxic and has required biocompatibility (Fig. 14). There are several original papers focused on UV and visible light-induced synthesis of hydrogels based on various synthetic and natural polymers [148–154]. Huang and coworkers reported an ultraviolet light irradiation technique to prepare gold or silver nanoparticles in carboxymethyl chitosan solution and observed that the solution worked as both reducing agent for cations and stabilizing agent for nanoparticles [155, 156]. Kumar et al. [157] synthesized Ag clusters by reduction of Ag^+ in polyvinyl alcohol hydrogel using gamma irradiation [157]. Radiation-induced synthesis is also useful for the reduction of metal salts in a hydrogel solution [158]. A review of radiation-induced synthesis of hydrogels and their applications in various fields is given in Table 1.

Table 1 Radiation-induced preparation of hydrogels and their applications in various sectors

S. No.	Hydrogel	Types of radiation	Applications	Ref.
1	Gg-cl-poly(acrylic acid-aniline)	Microwave	Water retention and dye adsorption	[32]
2	Gum ghatti/methacrylic acid/aniline	Microwave	Colon-specific drug delivery	[34]
3	Nanocellulose composite	Electron beam	Biorefining	[159]
4	Butyl methacrylate and acrylamide onto low-density polyethylene	γ -radiations	Wastewater treatment	[160]
5	Poly(ethylene glycol)/acrylic acid	γ -radiations	Site-specific drug delivery	[161]
6	Polyelectrolyte-cross-linked hydrogel	γ -radiations	Oral delivery of insulin	[162]
7	Starch/(EG-co-MAA)	γ -radiations	Various applications	[163]
8	Poly(vinyl pyrrolidone), poly(ethylene glycol), and agar	γ -radiations	Wound dressings	[164]
9	PVA/MAAc/gelatin copolymer	γ -radiations	Wound-healing applications	[83]
10	Natural polysaccharides blend-grafted acrylamide	Microwave and ultraviolet	Drug delivery systems	[165]
11	Carboxymethylcellulose/starch superabsorbent	γ -radiations	Pure polyelectrolyte-based superabsorbents	[89]
12	Acrylic acid (AAc) and 2-hydroxyethyl methacrylate (HEMA)	γ -radiations	Removal of acid dye	[90]
13	Tragacanth gum-based sterile hydrogel	γ -radiations	Drug delivery and wound dressings	[92]
14	Tragacanth gum-cl-PVA-co-PVP-based hydrogel	γ -radiations	Wound dressing	[93]
15	Psyllium and acrylic acid-based polymeric networks	γ -radiations	Selective absorption of water from different oil–water emulsions	[166]
16	Tara gum/acrylic acid	γ -radiations	Diaper applications	[167]
17	Kappa-carrageenan/acrylamide	γ -radiations	Agricultural purposes as a material for sodic soil remediation	[168]
18	Poly(acrylic acid) modification of <i>Cassia javanica</i> seed gum	Microwaves	Heavy metal ions removal	[98]
19	Polyacrylamide-grafted gum ghatti	Microwaves	Flocculant	[100]
20	Guar gum with acrylamide	Microwaves	Colonic drug delivery	[104]
21	Polyacrylamide-grafted gum acacia	Heavy ions	Sorption of methylene blue	[142]

6 Conclusion

As mentioned earlier that the main concern of this chapter is about the synthesis of polysaccharide-based hydrogels, however, fabrication and characterization of some selectively graft copolymers are need to be further explored. It is reported that components of such graft copolymers had functioned as smart materials. Therefore, it can be used for the advancing sensor and actuators technologies. The scientific community is putting tremendous efforts to enhance the properties of hydrogels and expected that the overall performance could be increased in near future in terms of better swelling capacity, biocompatibility, and biodegradability.

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