ijlpr 2021; doi ijlpr 2020; doi 10.22376/ijpbs/lpr.2021.11.2.P35-42

International Journal of Lifescience and Pharma Research

Review Article

Pharmaceutical analysis for Novel drug formulation

A Current Review on Polymeric Hydrogel Based Approach for Skin Tissue Regeneration.

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Abstract : Skin tissue defects have become one of the major sources of mortality and morbidity among all age group people worldwide. Skin tissue engineering has enticed considerable heedfulness from researchers as an optimistic approach for repairing partial/ full thickness burn tissue. Skin is a highly vascularized, bio mineralized composite material composed of fibroblasts and collagen surrounded by specialized extracellular matrix with high mechanical strength and structural complexity. Although the auto grafts and allografts were regarded as the high attainment for wound repair, the approach was limited due to their inability revascularize and mimicking the damaged tissue. Further, the Polymeric hydrogels are very attractive skin tissue engineering scaffolds. The structural similarity of the polymeric hydrogels to the skin extracellular matrix provides additional benefits for non-invasive tissue repair. Owing to their poor healing ability, tissue regeneration was found to be challenging in skin tissue defects. However due to its excellent moisture retaining capabilities, biocompatibility and biodegradability several researchers shown considerable interest in potential applications of the hydrogels for skin tissue repair.Furthermore, recent progress involves the development of hydrogels with ideal mechanical and fast stimulus responsive characteristics. Moreover, hydrogels with structural similarity to the skin extracellular matrix up regulate the cell material interactions for quicker skin tissue repair and more regulated stimulus response changes in the microenvironment. This current review focused on the applications of both the synthetic and natural polymers involved in the formulation of the hydrogels for the skin tissue regeneration. Furthermore, understanding the polymers simultaneously reducing the complexity of building hydrogels should be the aim of the future research in the skin tissue regenerative medicine field.

Key words: Hydrogel, Collagen, Gelatin, silk fibroin, Alginate, Chitosan.

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Recieved On 25 March 2020
Revised On 08 May 2020
Accepted On 06 July 2020
Published On 03 April 2021

Funding This Review did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation J. Subin Kiruba, Uppuluri Varuna Naga Venkata Arjun, Shanmugarajan T.S.* , A Current Review on Polymeric Hydrogel Based Approach for Skin Tissue Regeneration..(2021).Int. J. Life Sci. Pharma Res.11(2), P35-42 http://dx.doi.org/ijlpr 2020; doi 10.22376/ijpbs/lpr.2021.11.2.P35-42

1. INTRODUCTION

In case of skin tissue engineering concepts, a detailed study of the biology of the skin and its extracellular matrix is crucial for successful tissue regeneration and differentiation. Skin is a highly vascularized, bio mineralized composite material composed of fibroblasts and collagen surrounded by specialized extracellular matrix with high mechanical strength and structural complexity.[1-4] Skin tissue defects have become one of the major sources of mortality and morbidity among all age group people worldwide. Although the auto grafts and allograft were regarded as the high attainment for wound repair, the approach was limited because of their unwanted effects (i.e. their inability to revascularize and mimicking the damaged tissue). Therefore, skin tissue engineering has enticed considerable heedfulness from researchers as an optimistic approach for repairing partial/ full thickness burn tissue.[5-12] Moreover in the current review, various hydrogels with optimum biocompatibility and biodegradability have been widely investigated for use in skin tissue engineering. However, the biomaterials meant for the formulating the hydrogels, Collagen, Gelatin, Silk fibroin, Alginate, and Chitosan were found to be promising for skin tissue engineering. Further, Figure 1.Represents the characteristics and physiological applications of the hydrogel and Figure 2. Represents the role of hydrogels on burnt wounds.[13-18]

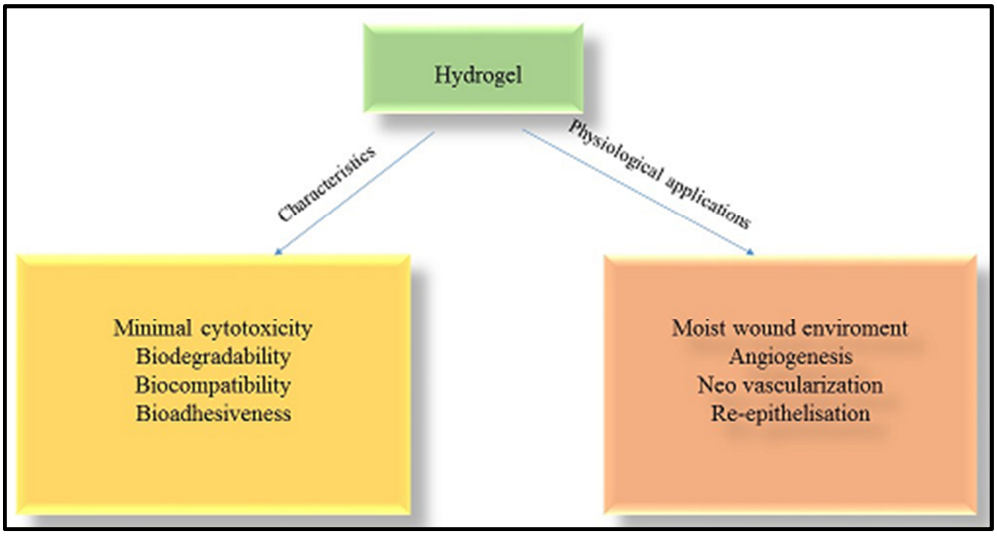

Fig 1. Represents the characteristics and physiological applications of the hydrogel

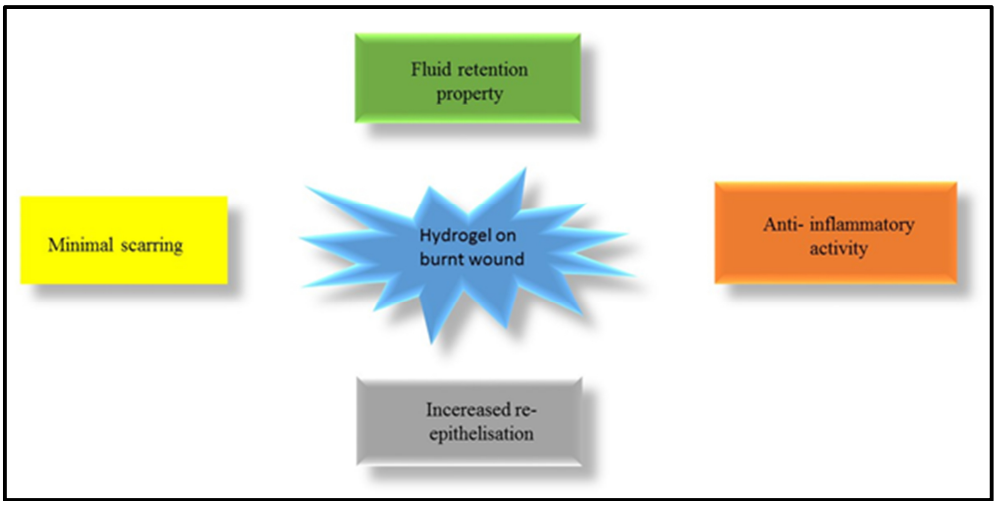

Fig 2.Represents the role of hydrogels on burnt wounds.

1.2. BIOMATERIALS USED IN SKIN TISSUE ENGINEERING

1.2.1. Collagen

Nilforoushzadeh *et al* given the abundance of skin replacements on the world market, the most important structure is the introduction of skin appendages and vascular networks as the major hurdles in creating more complex tissues. Moreover, they discussed for the first time, in a clinical feasibility study, aboutthe use of autologous dermal-epidermal skin grafts with intrinsic vascular plexus. The preliminary data (i.e. cell viability and Immuno histochemical staining) suggested that SVF-based full-thickness skin grafts are healthy and accelerate the process of wound healing. The next step of the study is a full-scale, randomized clinical trial for treating chronic wound patients [1].Bioprinted skin fastened the closure of wounds in full thickness by facilitating the development of epidermal barriers, without increasing contraction. Histological findings revealed that human cells from the bioprinted skin were incorporated, and that the wound formed the most similar epidermal barrier and extracellular matrix to normal, healthy skin. Jorgensen *et al*in his study, described that re-epithelialization and natural

collagen remodelling played a crucial role in aiding the bioprinted skin for the full thickness wound healing. Moreover, the human cells incorporated in bioprinted skin promoted a balanced collagen network of basket weaves. Furthermore, this remodeled skin was structurally and functionally similar to human skin. However, in order to increase the future bioprinting skin research, these methods and findings can be used to direct further study of collagen remodeling by tissue-engineered skin products. Eventually, this skin bioprinting technology could turn human patients with the ability to recapitulate natural collagen remodeling in full-thickness wounds into a new treatment for full-thickness wounds[2]. Zhang et al in his study, revealed about the importance of the serine protease inhibitor (SERPIN), Serp-1 in the mice cutaneous wound model. Further in this study, the Serp-1 loaded chitosan-collagen hydrogel enhanced wound healing by blocking the plasminogen activator (uPAR) type urokinase antibody. Furthermore, on 15th day Serp-1 loaded hydrogel treated mice shown ideal wound healing with excellent revascularization, reepithelization and collagen content [3]. Collagen hydrogels used as wound dressings have been shown to be gas and water permeable and have been shown to be a less effective bacterial barrier than occlusive dressings. It is for this reason that methods are required to mitigate bacterial wound infection and to promote wound healing. Olivetti *et al* developed a hydrophobic wound dressing to add simvastatin, which has potential applications for ulcer treatment and wound infection prevention. This was consistent with the DDSA-collagen swelling test, in which water absorption was 5.2 g / g for collagen and 1.9 g / g. Furthermore, studies were conducted on viability and adhesion. Cell adhesion in DDSA-collagen decreased by ~11 percent and the number of viable cells showed a tendency to decrease as the concentration of DDSA rose but was only significantly lower than 12 percent concentrations. Simvastatin filled modified gels, showing higher adsorption efficiency and lower release. Eventually, the DDSA-collagen materials have been evaluated for antimicrobial and anti-inflammatory activity. DDSA collagen hydrogels, either unloaded or charged with simvastatin, demonstrated sustained antimicrobial activity against Pseudomonas aeruginosa and Staphylococcus aureus for 72 hr likely due to the hydrophobic interaction of DDSA chains with bacterial cell walls. In conclusion, products, DDSA-collagen gels and collagen hydrogels. Simvastatin showed antimicrobial and anti-inflammatory properties in 2009 which make them promising for cutaneous wound cure. DDSA collagen hydrogels have exhibited better mechanical properties and lower degradation levels and the potential for water-insoluble drugs to act as drug carriers [4]. Skin replacements are one of the major skin loss remedies, and the best treatment choice would be a skin replacement which is readily available. Most cell-based skin replacements, however, require long production times, and thus patients endure long waiting times. The secreted proteins from the cells and tissues play vital roles in the promotion of wound healing. The fabrication by Maarof *et al* , an in vitro 3D model of DFCM-fortified collagen hydrogel showed that this construction is degradable where it releases proteins to the wound region. In vitro and in vivo research showed that this model do not cause an immunogenic response, has low immunogenicity or no immunogenicity and is suitable for clinical use in humans. Further Fibroblasts from human skin samples were grown using serum-free keratinocyte-specific media (KM1 or KM2) and serum-free fibroblast-specific media (FM), respectively, to obtain DFCM-KM1, DFCMKM2, and DFCM-FM. The 3D skin patch was acellular, flexible, semi-solid, and translucent. Collagen mixed with DFCM-KM1 and DFCM-KM2 demonstrated higher protein release relative to DFCM-FM plus collagen. Testing in vitro and in vivo showed that DFCM and hydrogel collagen did not cause an immune response. The implantation of the 3D skin patch on the dorsum of BALB / c mice with or without DFCM demonstrated a significantly faster healing rate compared to the no-treatment group 7 days after implantation, and all groups had full re-epithelialization at day 17. Such results demonstrate the possibility of using fibroblast secretory factors in an acellular 3D skin patch, together with collagen hydrogel, which can be used allogeneic ally for the immediate treatment of skin loss of full thickness [5]. Table 1.Demonstrates the role of collagen in formulations meant for skin tissue regeneration.

Table 1. Demonstrates the role of collagen in formulations meant for skin tissue regeneration.

Sl. No	Author	Polymer used	Application	References
1.	Jorgensen *et al*	Collagen	Re-epithelialization and Remodeling of the damaged skin tissue defects	2
2.	Olivetti *et al*	Collagen	Higher adsorption efficiency and lower release	4
3.	Maarof*et al*	Collagen	Biodegradable and releases proteins into wound regions.	5.

1.2.2. *Gelatin*

Because of their inflexibility and the slow formation of the protective film on the wound, self-healing hydrogels as wound dressings still face challenges in infection prevention, and in particular in dressing mass wounds. The design of a spray-filming (rapid-forming) hydrogel which can serve as a bacterial barrier is therefore of particular importance in the creation of wound dressings. Du *et al* developed an adipic acid dihydrazide modified gelatin (Gel-ADH) and monoaldehyde-modified sodium alginate (SA-mCHO)-based self-healing hydrogel. The hydrogels exhibit excellent self-healing properties through dynamic, Schiff base bonds. In addition, the gelation time of SAmCHO / Gel-ADH (SG) hydrogels is reduced to 2–21 s, leading to easy filming by spraying the two precursor solutions. Therefore, the rapid spray filming technology could provide enough versatility and speed to deal with mass and irregular wounds. Notably, experiments with bacterial barriers show that the SG hydrogel films could be an effective barrier for 12 h for Staphylococcus aureus and Candida albicans. SG hydrogels could therefore be used in wound dressings and they show great promise in mass-related applications and frequent traumas [6]. Reactive oxygen species (ROS) over expression leads to the pathogenesis of various diseases such as atherosclerosis, myocardial infarction, cancer, and chronic inflammation; The production of materials which can control local adverse effects resulting from excessive ROS generation

is therefore of great importance. Thi *et al* in his analysis, gelatin-hydroxy phenyl propionic (GH) hydrogels were inserted into the antioxidant gallic acid-conjugated gelatin (GGA) to build an injectable hydrogel with improved free radical scavenging properties compared to pure GH hydrogels. The modified hydrogels were quickly formed by a cross-linking reaction with high mechanical strength and biodegradability that was catalyzed by HRP. The resulting GH / GGA hydrogels effectively scavenged the hydroxyl radicals and DPPH radicals, and varying concentrations of GGA could modulate the scavenging power. In addition, the GH / GGA hydrogels will inhibit intracellular ROS development and protect hDFBs from damage to H2O2-induce high concentration oxidative stress between 0.75 and 1 mM. Further, GH / GGA hydrogels in particular enhanced wound healing by effectively promoting tissue regeneration, which was characterized by thinner epidermal thickness, increased blood vessel and hair follicles density, and higher collagen deposition and fiber alignment. Given these characteristics, the GH / GGA hydrogels produced in this study demonstrates potential in various biomedical applications, including wound treatment and tissue regeneration, where ROS oxidative damage is involved [7]. Hydrogels can be useful tools to promote wound healing, since they adhere to irregular wound shapes and act as a temporary matrix during healing. Nevertheless, the lack of inherent pore structures of most injectable hydrogels prevents desired interactions with surrounding tissue cells which limit their clinical effectiveness. Here Hou *et al* introduced a fast, cost-effective and highly biofunctional macroporous hydrogel injectable made from gelatin microgel scross linked by microbial transglutaminase (mTG). Pores are formed between the microgels by interstitial space. To produce gelatin microgels of an average diameter of 250μm, a water-in-oil emulsion technique was employed. The microgels clung to each other when cross linked with mTG to form a bulk hydrogel with inherent pores wide enough for cell migration. The porous hydrogel's viscoelastic properties were identical to those of nonporous gelatin hydrogel, formed by adding mTG to a homogenous gelatin solution. The porous hydrogel assisted higher cellular proliferation of human dermal fibroblasts (hDFs) over two weeks than the nonporous hydrogel, and allowed hDFs to migrate into the pores. Conversely, the hDFs could not permeate the nonporous hydrogel's surface. To show its possible use in wound healing, mTG inserted the gelatin microgels into a cut-out portion of an excised porcine cornea. The elastic hydrogel stably adhered to the corneal tissue for two weeks because of the action of mTG. Confocal images showed that the porous hydrogel migrated a significant number of cells from the corneal tissue into the interstitial space. The porous hydrogel was also used for platelet derived growth factor (PDGF) controlled release, increasing the proliferation of hDFs compared to the nonporous hydrogel. Finally, a porous hydrogel infused gelatinmicrogel will be a valuable tool for wound healing and tissue engineering [8]. Table 2.Demonstrates the role of gelatin in formulations meant for skin tissue regeneration.

Table 2. Demonstrates the role of gelatin in formulations meant for skin tissue regeneration.

Sl. No	Author	Polymer used	Application	References
1.	Du *et al*	Gelatin	Shows excellent self-healing properties through dynamic, Schiff base bonds.	6
2.	Thi*et al*	Gelatin	Enhanced free radical scavenging properties.	7
3.	Hou*et al*	Gelatin	Develops highly bio functional macro porous scaffolds, with excellent pore size.	8

1.2.3. Silk fibroin

Silk fibroin (SF) has gained importance in promotionof skin tissue regeneration, for its therapeutic effects against hypertrophic scar. Li*et al* prepared SF-based hydrogels (SFHs) with different concentrations of SF (1.5%, 3%, and 6%) and characterized their physicochemical properties. Cell experiments showed that in-vitro biocompatibility of these SFHs was favourable. More animal experiments in rabbits showed that the SFH (3 percent)-treated group developed thinner and slightly lighter color scars on their ears relative to the negative control group. In addition, treatment with SFHs decreased stiffness and led to collagen fibers being orderly organized. Moreover, the therapeutic effects of SFHs were revealed about the decreased levels of expression of α-smooth muscle action and this in turn minimised the wound healing duration. Furthermore, these findings are the first to demonstrate that SFH can be used for the treatment of hypertrophic scars as an important therapeutic agent[9]. Napavichayanun *et al* High-Pressure CO2 system used to prepare fibroin / PVA hydrogels with and without sericin in his research. The physical and mechanical properties of the hydrogels revealed about the crosslinking capability, melting enthalpy, chemical structure, swelling and biodegradability of these developed hydrogels. Finally, due to its excellent water retention characteristics this hydrogel was proved to be a ideal formulation for skin tissue regeneration.[10] Hydrogels developed from silk fibroin (obtained from Bombyx Mori cocoons) demonstrated the significant wound healing characteristics because of its excellent biocompatibility and biodegradability characteristics. He et al developed a heparin-immobilized fibroin hydrogel to deliver FGF1 (human acid fibroblast growth factor 1) on top of wound in rats with complete thick skin excision by carrying out extensive preclinical studies to completely assess their safety and effectiveness. Compared with the commonly used chitosan, the wound-healing performance of established fibroin hydrogels was evaluated in the full thickness wound model of rats [11]. A significant health risk is full-thickness skin wounds, consistent with severe burns or chronic wounds. Here, Chouhan *et al* documented the production of in situ forming hydrogel using a natural silk fibroin (SF) biomaterial to treat burn wounds. Blends of Bombyxmori and Antheraea assama isolated SF solutions demonstrates inherent self-assembly between silk proteins and leads to irreversible gelation at body temperature. Investigation of the gelation process shows crosslinking as a result of β-sheet structures being formed as analyzed by X-ray diffraction and Fourier transforming infrared spectroscopies. The SF hydrogel supports the proliferation of primary human dermal fibroblasts and the migration of collagen gel-like keratinocytes (Col) as examined under in vitro conditions.

The SF hydrogel also provides the full-thickness of third-degree burning wounds in vivo with an instructive and supporting matrix. A 3-week comparative study with Col indicates that SF hydrogel not only facilitates wound healing but also demonstrates changes from inflammation to proliferation, as shown by the expression of TNF-α and CD163 genes. Additionally, the deposition and remodeling of type I and III collagen fibers suggests an enhanced overall tissue regeneration. The SF hydrogel shows comparable results with Col as an efficient and affordable solution towards a possible therapeutic strategy for burn wound care [12]. Table 3. Demonstrates the role of silk fibroin in different skin based formulations.

Table 3. Demonstrates the role of silk fibroin in different skin based formulations.

Sl. No	Author	Polymer used	Application	References
1.	Li *et al*	Silk Fibroin	Decreased stiffness and led to orderly organization of collagen fibres.	10
2.	He *et al*	Silk Fibroin	Promoted in vitro adhesion and proliferation of a variety of human cells.	11
3.	Chouhan*et al*	Silk Fibroin	Demonstrated inherent self-assembly between silk proteins and lead to irreversible gelation at body temperature.	12

1.2.4. *Alginate*

Injectable hydrogels are very useful technologies for non-compressive wound care applications. Nonetheless, the manufacture of mechanically robust hydrogel products with inherent functionalities in both hemostatic regulation and wound healing remains difficult without additional growth factors supplements. Here, Zhai*et al* documented the combination of a cell adhesive peptide conjugate (Pept-1) and alginate (ALG) to confer supramolecular hydrogels with excellent mechanical properties and high efficacy in both hemostatic and wound healing without requiring additional growth factors.The Pept-1 and ALG co-assembly process, controlled by electrostatic interactions and metal chelation, provided a composite hydrogel with denser nanofibrillar structures and improved mechanical strength when compared with the Pept-1 gel alone. As-prepared Pept-1/ALG hydrogels showed excellent injectability and thixotropic properties making them perfect wound dressing materials. When spiked with whole blood in vitro, the composite hydrogel induced strong hemostasis and reduced the amount of bleeding in a liver puncture mouse model to B18 percent of untreated function. In the meantime, it stimulated adhesion and migration of NIH3T3 fibroblast cells in vitro, and increased the rate of wound healing in a mice model of full-thickness skin defect. Additionally, the hydrogel Pept-1/ALG demonstrated excellent biocompatibility with no apparent hemolyticbehavior. The technique of using co-assembled nanostructures made up of biofunctional peptides and polysaccharides could be further used in the future in order to create a wide range of nanocomposite materials for a variety of biomedical applications [13]. Treatment of large acute or chronic wounds remains a challenging task due to a lack of effective methods to accelerate healing of wounds. Although growth factor-based wound products are found to be effective, they are expensive and potentially associated with increased mortality from cancer. Here, they designed a new antioxidant-embedded hydrogel system to speed up the wound healing process. They prepared multifunctional poly (vinyl alcohol)/sodium alginate (PVA / SA) hydrogels containing 5-hydroxymethylfurfural (5-HMF) and silver nanoparticles (Ag-NPs) and investigated their physichemical and biological properties in vitro and in vivo. PVA, SA, 5-HMF, and Ag-NPs respectively were used for good mechanical properties, good biocompatibility, anti-inflammation, and antibacterial activity. 5-HMF is commonly present in many foodstuffs (such as honey, coffee and black garlic) and is known as antioxidants. In the case of Kong*et al*in vitro study, 5-HMF was found to effectively promote human skin fibroblast (HSF) proliferation and migration, and collagen production. In addition, 5-HMF-embedded PVA / SA hybrid hydrogels supported controlled release and good cell compatibility, and more importantly, enhanced in vivo wound healing through reduced inflammation, increased angiogenesis / vascularization, Increased production of collagen, and facilitated re-epithelialization [14]. Due to its excellent moisture retention property hydrogels played a significant role in skin tissue regeneration. Consequently, Shi *et al* standardised alginate / CaCO3 composite microparticles (almost 430 μm) with adjustable compositions for sustainable drug release and pH sensitivity were manufactured successfully using microfluidic technology. Lyophilized composite microparticles reverted to hydrogel state after rehydration due to the presence of CaCO3 and the strong interactions with alginate molecules. However, for the same type of microparticles the release rate at pH 6.4 (simulation wound microenvironment) was always slower than that at pH 7.4. Rifamycin and the basic fibroblast growth factor (bFGF) were separately encapsulated in AD-5-R and AD-40-F to achieve a rapid release of rifamycin and a slower, more sustained release of bFGF, respectively; CD-F-R was a mixture of AD-5-R and AD-40-F at weight ratio 1/1. Inhibition zones S, for AD-5-R and CD-F-R. Aureus exhibiting a sustained antibacterial property were observed until Day 5. Based on the NIH-3T3 cell micropattern in vitro wound healing model on glass covers with a whole array, it was found that AD-40-F and CD-FR have significantly stimulated cell proliferation and migration rates. CD-FR microparticles substantially improved wound healing in a full-thickness skin wound model of rats, with higher granulation tissue thickness and greater bioactivity to induce angiogenesis than the control group. In addition, microparticles from CD-FR demonstrated good in vivo biocompatibility and biodegradability. CD-F-R microparticles greatly improved wound healing in a full-thickness skin wound model of rats, with higher granulation tissue thickness and greater bioactivity to induce angiogenesis than the control group. In addition, microparticles from CD-F-R demonstrated good in vivo biocompatibility and biodegradability. Taken together, CD-F-R composite microparticles during wound healing can ideally meet the requirements for different stages and have demonstrated a good potential to be used as dressing materials [15]. Table 4. Demonstrates the role of alginate in different skin based formulations.

Table 4. Demonstrates the role of alginate in different skin based formulations.

Sl. No	Author	Polymer used	Application	References
1.	Zhai*et al*	Alginate	Promoted excellent mechanical properties and high efficacy in both hemostatic and wound healing without requiring additional growth factors	13
2.	Kong *et al*	Alginate	Supported controlled release and good cell compatibility, and enhanced in vivo wound healing through reduced inflammation, increased angiogenesis / vascularization.	14
3.	Shi *et al*	Alginate	Demonstrated good in vivo biocompatibility and biodegradability	15

1.2.5. Chitosan

Effective treatments of severe skin loss, where lack of angiogenesis is a major obstacle, urgently need it. Jing *et al* presented in this study a thermosensitivethiolated chitosan (CSSH) hydrogel combined with Histatin1 (Hst1) as a wound dressing to test its effectiveness in enhancing cell adhesion, spread, migration, and angiogenesis. The composite hydrogels showed a sustained release of Hst1, with a gelation time of 5 to 7 min. Cell culture indicated that HUVECs were promoted to adhere, spread, migrate, and form tubules, especially for the Hst1-H Group. The in vivo healing assessment showed that the recovery rate in the Hst1-H group improved to 84 percent at day 7, and the positive CD31 cells, vascular endothelial growth factor (VEGF) positive cells and associated collagen fibres were significantly greater than the regulated groups. Here Wenbo *et al* reported an easy approach for chitosan -heparin hydrogels with controlled mode of release and their intrauterine adhesion applications. The precursor to sol has been transformed in 15 minutes to gel at physiological temperature. Due to the noncovalent bond cross-linking of the composition s, biopolymer-based hydrogels were successfully prepared through a mild cycle. The hydrogels showed good stability in either DMEM or PBS solution in vitro, with maximum degree of swelling (20 percent) occurring 3 days after formation. BSA's release profiles loaded and SDF -1α loaded hydrogels showed that 71.2 percent of BSA was released within 5 days in a controlled manner and 53 percent of SDF -1α was released. In situ drug delivery in injured rat uterus showed SDF-1α controlled release of hydrogels correctly restoring the injured uterus, after 7 days of treatment the uterus showed no statistical difference with normal morphology and physiology. This hydrogel could be a candidate for cure for uterine injury and other drug delivery methods for wound dressing [16]. In case of some hydrogels lack of bioadhesiveness and mechanical characteristics limited their importance in skin tissue regeneration. Here, Xue*et al* developed a multifunctional quaternized chitosan-matrigel-polyacrylamide (QCS-MPAM) hydrogel. The hybrid hydrogel was investigated in vitro and vivo for morphology, swelling ratio, mechanical check, antimicrobial ability, hemostatic efficiency, and biocompatibility. The hybrid hydrogel exhibited a three-dimensional (3D) microporous structure, high swelling ratio, and excellent stretchable and compressive strength, close module to human skin, good adhesiveness and low cytotoxicity. The findings of in vivo histology and molecular testing showed that the hybrid hydrogel could significantly enhance wound healing, collagen deposition, and induce skin adnexal regeneration by upregulating anti-inflammatory factors and pro-inflammatory factor downregulation. Together, the present antibacterial hydrogels with hantatic and adhesive properties are known to have promising potential for the full-thickness skin defect being used as wound dressings [17]. The ideal candidate for wound healing is an injectable hydrogel dressing with multifunctional properties of superior hemostasis, antibacterial action, tissue adhesive and cytocompatibility. Du*et al* developed a novel hydrogel dressing consisting of hydrophobically modified chitosan (hmCS) and oxidised dextran (OD), in this research. It was distinguished by gelation time, microstructure, injectability, self-healing, and rheological properties. It was confirmed the in vitro capacity of the hydrogel precursor solution to coagulate whole blood heparinized. The haemostatic activity in vivo was demonstrated in a liver model that haemorrhages rats. The antibacterial activity of S. Aureus and P. aeruginosa were tested in vitro by an antibacterial surface examination. The corresponding killing efficiencies at a bacterial concentration of 108 CFU / mL were up to 95.0 per cent and 96.4 per cent. Co-culturing with 3 T3 fibroblast cells tested the cytotoxicity. The wound healing functions were further tested with a sample of rat skin contaminated with infection. The above findings showed that the hydrogel with multifunctional activity has potential for healing of hemorrhagic and contaminated wounds [18]. Table 5. Demonstrates the role of chitosan in different skin based formulations.

Table 5. Demonstrates the role of chitosan in different skin based formulations.

Sl. No	Author	Polymer used	Application	References
1.	Wenbo*et al*	Chitosan	Excellent stability and controlled mode of release	16
2.	Xue*et al*	Chitosan	Shown high swelling ratio, excellent compressive strength, good adhesiveness and low cytotoxicity.	17
3.	Du *et al*	Chitosan	Shown excellent potential for healing of hemorrhagic and contaminated wounds	18

2. CONCLUSION

The outcome of the skin tissue repair was attributed to the skin extracellular matrix deposition and remodelling. If the rate of degradation was not adequate, extracellular matrix cannot be deposited in the skin defect region, thereby affecting the skin tissue regeneration. Moreover, hydrogels were considered as the ideal tissue engineering materials in skin tissue repair due to their optimized degradation rate and ideal biocompatibility. However, throughout recent decades, polymeric hydrogel scaffolds containing cells or drugs were commonly developed to facilitate the regeneration of the skin tissue defects. Moreover, the current review focused on the applications of both the synthetic and natural polymers involved in the formulation of the hydrogels for the skin tissue regeneration. Furthermore, understanding the polymers simultaneously reducing the complexity of building hydrogels should be the aim of the future research in the skin tissue regenerative medicine field.

3. ACKNOWLEDGMENTS

The authors are thankful to Vels Institute of Science, Technology & Advanced Studies (VISTAS), Chennai, for the facilities extended.

4. AUTHORS CONTRIBUTION STATEMENT

Conceptualization, writing was done by Shanmugarajan T.S. and UppuluriVaruna Naga Venkata Arjun whereas, review and editing were done by Shanmugarajan T.S.,Subin Kiruba and Uppuluri Varuna Naga Venkata Arjun. In general, all the authors had agreed to the publishing this review article.

5. CONFLICTING INTEREST

The authors report no conflicts of interest.

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