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REVIEW ARTICLE **OPEN ACCESS**

Current Prospects and Promises of Polymeric Hydrogels in Dentistry

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ABSTRACT
Tooth loss due to dental caries, periodontal diseases, chronic diseases, trauma and congenital anomalies necessitates regenerative approach in dentistry. The challenge of safe incorporation and delivery of these regenerative factors is being addressed by biomaterial scaffolds. It facilitates release of bioactive molecules at the site of implantation and delivery of substrates. Every year, it shows increasing commercially interesting uses, especially for dentistry application. This review focus on application and limitation of dental biomaterials hydrogel, Poly(lactic acid), Polyglycolic acid, Polylactide-co-glycolide, Poly (ε-caprolactone), Polyurethane, Polyacrylates, Polyvinyl Alcohol, Alginate, Chitosan, Cellulose, Collagen, Hybrid hydrogels and Injectable hydrogels. These dental biomaterials are required for the current dental treatment strategies.
Key words: Hydrogel, tooth regeneration, biomaterials, Scaffold, drug delivery biocompatibility and biopolymer.

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INTRODUCTION

The endogenous tooth regeneration at the desired site, prerequisites biological restoration of tooth components, connective and supportive structures, for which a combination of stem cells, growth factors and scaffold are inevitable components. The biomaterial scaffolds provide temporary anatomic matrices, which furnishes the biophysical support for cell recruitment, attachment, proliferation, differentiation and tissue synthesis [1].

In dentistry biomaterials serves as scaffold for cell adhesion, system for controlled drug delivery, vehicle for cell transplantation, tissue engineering for functional tissue replacement and also other materials such as dentine bonding, impression materials, glass ionomers, composites, luting cements and ceramics. The ideal biomaterials for dental applications need to satisfy the prerequisites like biocompatibility, strength, durability, non-toxicity, corrosion and aesthetics [2]. Biomaterials scaffolds instructs the behavior of adhered or encapsulated cells. Biomaterials used for biomedical applications are grouped into metals, ceramics, polymers, and composites [3]

Biodegradable polymeric biomaterials are mainly employed as temporary scaffolds for tissue healing and regeneration. Being loaded with cells, growth factors, and signaling molecules, these polymers can act as regenerative templates until a functional tissue is reformed. Their biodegradability can be exploited for its safer elimination from the body and to escape from chronic immune responses and they are highly recommended for bone and tooth regeneration [4].

HYDROGELS

Hydrogels are the first biomaterial designed for use in human body owing to their similarities with natural soft tissues, excellent biological performance, and inherent cellular interaction capability [5]. A hydrogel is a cross-linked polymer matrix that exhibits the ability to swell in water without dissolving and to retain a large volume of water within its three-dimensional structure. Hydrogels enables noninvasive surgical procedures using stem cell therapy principles to control stem cell functions. These are generally made from natural or synthetic polymers with higher hydrophilicity, which has found

promising applications in regenerative medicine in dental tissue engineering. Synthetic polymers are known for their properties like reproducibility, biocompatibility and tuned biodegradability rates. [6].
Several types of polymeric hydrogel scaffolds have been used to support growth and differentiation of progenitor cells for tissue regeneration, drug delivery, scaffold matrix, implants, tightening the microchannels in teeth [7]. Even though several polymeric biomaterials are being well appreciated for dental applications, only a few succeeded to be established in clinical applications. An ideal material should mimic the native extra cellular matrix (ECM) in both *in vitro* and *in vivo* environments. The ease of simultaneous delivery of cells, drugs, antibiotics, growth factors, and signaling molecules in a single application makes the polymeric biomaterials versatile for oral implant. But toxicity or acidity of hydrolytic products will eventually lead to inflammation and cytotoxicity [8].
Hydrogel scaffolds made of synthetic polymers are produced by a variety of fabrication techniques, which are manufactured into preformed sizes and shapes according to clinical requirements. Poly (lactic) acid, poly(glycolic) acid, PPF-derived copolymers, PEG-derivatives and PVA are few important synthetic hydrogel polymers currently used for dental pulp tissue engineering. Poly (ethylene oxide) (PEO), poly (propylene oxide), poly (acrylic acid) (PAA) and poly (propylene furmarate-co-ethylene glycol) (P (PF-co-EG) were being tried for repair of oral tissues [9]. The synthetic hydrogels have the advantages of finely-tuned properties such as degradation and mechanics, adjunct with high reproducibility. Biocompatibility of the material is closely linked to molecular weight of the degradation products. Undesirable features like uncontrolled or non-tunable biodegradation, toxicity of the byproducts, mechanical incompatibility, difficulties in sterilization, etc. pose the major disadvantages of polymeric materials [10]. The *in vivo* leaching of additives used during the fabrication of polymeric materials has been cited as a cause of inflammation leading to the eventual rejection of implanted biomaterials[11].
Poly (ethylene glycol) (PEG) based synthetic hydrogels are mostly used for dental regenerative applications [12]. Synthetic scaffolds are also used to deliver anti-inflammatory agents such as ibuprofen, dexamethasone, diclofenac, rolipram etc. Dental pulp progenitor cells attach to electrospun PEG scaffolds and have been transduced to form 3-D collagen structures [13]. Such scaffolds, which have been shown to support the regeneration of pulpal tissues, could also be used to deliver these or other anti-inflammatory molecules such as resolvins in order to control pulpitis, thereby facilitating pulpal repair. These polymers are attractive due to their handling properties and relative ease of production for endodontic regeneration.
Natural hydrogels are more preferred due to their innate biologic activity and native extracellular matrix mimicking property. Hydrogel polymers from natural origin widely used are collagen, gelatin, fibrin, HA, alginate, chitosan, hyaluronic acid. Though natural polymeric hydrogels lack mechanical strength as that of synthetic ones they are advantageous by virtue of their bioactive or bio-inert nature. Some of these materials significantly modulate cell phenotypes enabling anti-inflammatory effects where as few materials exists as bio-inert facilitating low protein and cell adsorption and also inhibition of monocyte differentiation. However, its response is mainly with respect to the microenvironment and its variability in molecular weight and confirmation during synthesis. Natural polymers like chitosan, alginate, amelogenins, collagen, and hyaluronic acids are implicated in dental pulp regenerative therapy [14].

POLY(LACTIC ACID)

Poly(lactic acid) (PLA) is a linear polyester comprising lactic acid monomers which can be synthesized by chemical means or derived from biological sources. Both L and D isomers of lactic acids are being employed for the synthesis of PLA with both products differing significantly in physiochemical and biological properties.
Generally, PLA is hydrophobic which constitutes its water insolubility, which can be co-polymerized with other monomers and can be subjected to functionalization with specific biological cues. Biocompatibility, biodegradation, mechanical properties, excellent transparency, and its renewable sources make PLA an ideal choice for dental applications. Still, lower degradation profile, immune challenge in the initial stage of implantation (acidic degradation products triggers inflammation) and chances of accumulation of crystalline hydrolysis products often offers a hurdle for the long term dental applications of PLA [15].
But the incorporation of a secondary material enabling the neutralization of acidic degradation products is in practice.Hu *et al.* fabricated an electrospun PLA scaffold membrane decorated with beta-tricalcium phosphate for dental applications which offered a good biological response and addressed much of these issues associated with PLA [16]. High molecular weight PLA in combination with phospholipid polymer bearing phosphorylcholine groups reduces thrombus formation. This notably reduces inflammatory cytokines IL-6, IL-1B, and TNF-A and has been used in cardiovascular stents. PLA based polymers enable sustained drug release. Functionalization of PLA with biomimetic cues can both minimize the side effects and improve the performance. PLA based hydrogels are tailored as thermo-responsive, stimulus

responsive and shape memory hydrogels. A few successful examples include ReGel® ((PLGA–PEG–PLGA) and 732 Genexol®-PM (PLA PEG).

POLYGLYCOLIC ACID

Polyglycolic acid (PGA) is a linear polyester and composed of glycolic acid monomers connected through ester linkages. PGA has been widely used as absorbable sutures and in orthopedic pins and screws. PGA mesh fabric is extensively used for reinforcing injured tissue. The ability of PGA to promote cell attachment and tissue development potentiates its biomedical applications. The acidic biodegradation products of PGA, namely, glycolic acid which dimerizes to form glycolide, offers risk for its dental applications [17]. If the biodegradation is controlled, the glycolic acid can enter the TCA cycle and can be cleared through kidneys. In case of uncontrolled biodegradation the glycolic acid accumulates beyond limits of metabolism and leads to a drop in pH of surrounding medium, leading to inflammation. PGA also induces adhesion due to inflammation because of decreased tissue pH and xenobiotic reaction after placement. Hence addressing these demerits is quite required for effective use in dental application[18]. PGA scaffolds have shown to support the adhesion and proliferation of pulpal fibroblasts.It is widely used as an artificial scaffold for cell transplantation and is a short lasting polymer which degrades as the cells excrete ECM[19].

POLYLACTIDE-CO-GLYCOLIDE

Polylactide-co-glycolide (PLGA) is a co-polymer of PLA and PGA. PLGA possesses most of the beneficial characteristics of both PLA and PGA in terms of its biodegradation, amorphous nature, and mold ability. PLGA are approved by FDA for drug delivery and are mainly exploited for carrying different types of drugs such as peptides, vaccines, peptides, proteins, and other micromolecules. The amount of lactic acid and glycolic acid content in PLGA determines properties of the polymer. So fine tuning of monomer composition is necessary depending on desired applications. A report showed that 50-50% PLGA was highly susceptible for hydrolysis [20]. Even though PLGA possesses certain favorable characteristics for bone and tooth applications, its hydrophobicity limits cell adhesion and subsequent tissue repair [21]. Moreover, the lower mechanical strength, higher flexibility, and poor osteoconductivity prevent PLGA from load bearing applications. Calcium phosphate cement (CPC) implants containing PLGA microparticles have been developed as bone implants where acidic degradation products are buffered by calcium phosphate. At the same time release of calcium and phosphorous ions can favor bone and teeth remineralization [22].

Still, the biocompatibility and immune compatibility promote PLGA an applicable candidate material for dental tissue [23]. Pulp-like tissue formation is seen in poly(lactic-co-glycolic acid) (PLGA), which is the copolymer of PGA and PLA, on seeding with dental pulp progenitor cells *in-vivo* conditions.

POLY (ε-CAPROLACTONE)

(PCL) is aliphatic polyester and has been used for several biomedical applications due to its semi-crystalline nature, solubility in a wide range of organic solvents, and thermal stability [24]. Its poor degradation rate limits its short term use but potentiates long term applications [25].The increased resistance offered by PCL against water, oil, chlorine, its excellent mechanical properties, superior osteoconductive effects and lower viscosity potentiates its application for dental regeneration.. Non-toxicity, tissue compatibility, and low cost propels PCL as polymer common among the dental biomaterials [26].

PCL can be a substitute for the conventional filling material gutta-percha. An ideal root filling material should be a predictable sealant, inhibit residual microbial proliferation, resist re-contamination, and promote the healing of the periapical region. PCL can be tuned to obtain all these qualities. *Ex vivo* root canal model studies have shown that the PCL excelled above the commonly used sealers like gutta-percha and zinc-oxide/eugenol systems. Also, the PCL was capable of sealing the root in an aqueous medium even without the application of a sealer [27]. PCL based dental filling material is now commercially available in the trade name Resilon™which substitutes for gutta-percha. Apart from PCL, Resilon™ also bears bioactive glass, bismuth oxychloride, and barium sulphate and possesses the same melting point of gutta-percha (60°C). A large set of similar experimental data suggest PCL to be an ideal choice for dental application especially as a filler/sealer [28].

POLYURETHANE

Polyurethane (PU) is a versatile class of polymers due to their moldability, injectability, extrusion capacity, and recycling. PU can be subjected to several structural modifications by simple chemical reactions. The acrylate modified PU is being used for dental applications [29,30], since a long time and PU based materials were reported to be successful as shock absorbers to reduce the stress on denture bearing tissues like teeth where such tissues are reported to undergo atrophy if they fail to bear stress. By placing a shock absorber lining between the denture prostheses and tissue, such a chance of atrophy can be minimized. The risk of toxicity using PU is higher due to leachable isocyanates[29]. Reports show that ROS/RNS action upon a biomaterial results in reduction in molecular weight of the polymeric implant, which also lead to material degradation. Surface crackings of polyurethane–based pacemaker have been reported, which led to insulation and structural damage of bioprosthetic heart valve. The induced antimicrobial properties and decreased polymerization shrinkage are added advantages of PU based dental materials[31].

POLYACRYLATES

Polymers based on acrylate are the most commonly used dental biomaterial. Majority of the polyacrylate is comprised of poly(methyl methacrylate) (PMMA) which is being used as dentures, crown materials and also in composites. Their polymerization can be initiated *in situ* by chemicals, light, free radicals, or heat. The lower mechanical properties, high chance for biofilm formation, and increased possibility for denture stomatitis are the major drawbacks associated with polyacrylates [32]. Co-polymerization and cross linking of polyacrylates with agents like butadiene styrene are reported to improve the mechanical strength. Phosphate containing ethylene glycol dimethacrylate as monomer for polymerization proved to be effective for preventing the bacterial colonization.Frictional wear and tear of polyacrylate based dental materials was effectively prevented by incorporating polytetrafluorethylene (PTFE) to the polymer matrix[33].

Biodegradation offers a hurdle for acrylate-based resins. The endogenous biochemicals in saliva including enzymes, polysaccharides, ions and the microbes along with exogenous dietary compounds interact with the acrylates and initiate their degradation, which is further increased by mechanical action of mouth. The surface and bulk degradation of these materials compromise their desired function by altering their chemical properties. Degradation products also elicit biological responses and may also further catalyze the degradation [34]. Novel strategies to address the disadvantages associated with polyacrylate dental materials are needed since these materials are extensively used in dentistry.

POLYVINYL ALCOHOL (PVA)

PVA is polyvinyl acetate derived synthetic polymer obtained via partial or complete hydroxylation. PVA shows high aqueous solubility but resistant to most organic solvents. The water solubility promotes PVA hydrogels by crosslinking for various applications and can be either chemically or physically crosslinked to gel form. The low protein adsorption property, hydrophilicity, swelling property and elasticity, chemical resistance, microporous structure, nontoxic, noncarcinogenic and biocompatibility projects PVA in various biomedical applications. Some of the most common medical uses of PVA are in soft contact lenses, eye drops, embolization particles, tissue adhesion barriers, as artificial cartilage, arteries, muscles and hydrophilic coatings to improve neurologic regeneration. The properties of PVA hydrogel are closer to human body cartilage tissue than that of other artificial materials[35].

Hydroxyapatite reinforced PVA is used for overcoming the shortcomings of poor mechanical strength and widely used in cartilage substitute materials and cartilaginous tissue regeneration.Bakerand co workers reported crystallization of PVA with a miscible organic solvent at low temperature increases its water content, tensile strength and favors low protein adsorption. The porous and soft tissue texture has been exploited for sustained and controlled therapeutic releases like painkillers, antibiotics, hormones, anti-cancer drugs vitamins [36]. In vivo studies showed that the lower wear particles in PVA bio-implants reduce inflammation rates owing to their nontoxicity towards macrophages [37]. Modification by crosslinking and functionalization with glutraldehyde, tetra ethylene glycol ditosylate improves mechanical strength and thermal properties of PVA making it suitable for various applications [38]. PVA blend with zwitterion polymeric films are being used in dentistry for reducing friction and wear of dental biomaterials.

ALGINATE

Alginate is a common natural biomaterial used in dentistry especially as dental impressions meant for indirect restorations. This poly anionic hetero polysaccharide from marine sea weeds exists in irreversible colloidal form [39]. Chemically, alginate is a block co-polymer of β-D mannuronic acid (M) and α-L guluronic acid (G) residues. Chelating with divalent metal ions alginate forms a hydrogel. The biological responses of alginate depend on relative contents of G and M residues in the polymer [39,40]. Alginate possesses high biocompatibility owing to their hydrophobic nature, lack of ability to adhere to the mammalian cell and poor enzymatic degradation. The reduced toxicity, biocompatibility and gelation in presence of divalent cations favor its wide application in drug delivery and tissue engineering. Ease of handling, reliability, simplicity, and low cost make alginate a comfortable material for dental patients. Alginate is generally anti-inflammatory in nature and high molecular weight alginate is known to reduce pro-inflammatory cytokines IL-1beta and IL-6. But contaminants like metal ions and biomolecules based impurities present in alginate elicit adverse responses [41]. Alginate is commonly used in preliminary impressions, temporary crown-and-bridge impressions, opposing dentition impressions, orthodontic models, and sports mouth guards [42]. Repeated impression taking during orthodontic pretreatment using alginate leads to cytotoxicity due to the greater absorption potential of oral mucosa. The poor mechanical and dimensional stability add additional challenges for its consistency which demands the incorporation of zinc, barium, cadmium, lead silicates and fluorides. [41,43]. The hydrogels are compatible with mesenchymal progenitor cells derived from the gingiva and periodontal ligament, which upon loaded with TGFβ1, induces odontoblast-like cell differentiation in a human tooth slice model.

Chitosan

Chitosan is also a polysaccharide biomaterial widely used in dentistry due to its inherent antimicrobial properties and nontoxic nature. Chitosan is derived from chitin,which is abundant in crustaceans, insects, fungi, and algae. The limited water solubility of chitosan hinders its wide spread application in dentistry as chitosan needs a mildly acidic medium for solubility [44]. Water-soluble derivatives of chitosan were previously synthesized and proved to display excellent antimicrobial effects against a wide range of cariogenic organisms

Reports show that chitosan significantly increases the M2 macrophage polarization and secretes anti-inflammatory cytokines such as IL-10, IL-12 and TGF-beta1within short span of implantation. Itactivates ERK1/2 (extracellular- signal-regulated kinases) pathway leading to gingival fibroblast proliferation contributing to tissue reconstruction [45]. Fibroblast responses to chitosan are heavily influenced by chemical modification and mechanical properties and their proliferation and infiltration positively related to the swelling ratio.

The anti-inflammatory potential of chitosan was exploited for treating periapical lesions during root canaling. Chitosan mediated IL-8 release, chemotaxis of inflammatory cells, angiogenesis, and ECM reorientation made immense opportunities in biological pulp treatment. Furthermore, D-glucosamine, the monomeric unit of chitosan, was reported to elicit a wound healing effect which signifies its application in dental pulp capping medicament [46]. The wound healing activity of chitosan is mainly due to secretion of TGF-Beta and platelet derived growth factor (PDGF) from macrophages. The ability of chitosan to chelate metal ions can limit the continuous flushing of cleaning solutions like EDTA and hypochlorite [47]. However, loading chitosan with drugs or chemokines enables modulation of cellular responses. Hence, these versatile qualities along with excellent biocompatibility, biodegradation, and bioadhesion promote chitosan as a promising biomaterial for dental applications.

Cellulose

Cellulose is the most abundant natural polymer, composed of glucose monomers linked through 1,4-beta glycosidic linkages. The presence of ample –OH groups and resulting abundance of H bonds confer stability and strength to cellulose [48]. The cellulose and its oxidized derivatives have been used for dental applications especially as a hemostatic agent. On contact with blood, the cellulose forms a gelatinous mass that mimics a blood clot. Moreover, the lower pH of cellulose based biomaterials can elicit antimicrobial effects [49]. Carboxymethyl cellulose was proven to be an effective dental gel for the delivery of hydroxyapatite to the dentine tubules for reducing the hypersensitivity [50]. Exceptional biocompatibility and low cost are added benefits to cellulose based dental biomaterials.

Collagen

Collagen is the most abundant protein in animal system and represents the major portion of connective tissues. Collagen is composed of 3 polypeptide chains each with thousands of amino acids and a stretch of Gly-X-Y (X and Y can be any amino acid, proline and hydroxyproline). Being a biomaterial, the collagen has been hailed for its biocompatibility and its osteoconductive nature which is crucial for the regeneration and repaid of both bone and teeth [51]. The natural tooth is a complex of collagen and hydroxyapatite so incorporation of hydroxyapatite in collagen based scaffolds/composites can improve their performance. Such a complex of collagen and hydroxyl apatite has been considered as the most biomimetic system for osseous tissue repair [52] . The presence of collagen guides the cells to proliferate on surface of hydroxyl apatite and enhance bone and tooth regeneration [53]. In dentistry, collagen has a established rate of success as GTR (Guided Tissue Regeneration) membrane, which allows selective proliferation of periodontal ligament cells as well as fibroblast chemotactic. Collagen also is a well-known root-conditioning agent, which enhances fibroblast attachment and migration of periodontal cells to root surfaces. Type 1 collagen supports new tissue growth during wound repair cycle and pulpal preservation [54].

Hybrid hydrogels

In order to utilize the advantages of natural hydrogel like biocompatibility and mechanical strength of a synthetic material, both the natural and synthetic hydrogels are coupled to form a hybrid implant material. The hybrid and composite hydrogel systems can be fabricated by incorporation with inorganic phases like hydroxyapatite, bio glasses and calcium phosphate and/or blending of two different polymeric materials into a unifying hydrogel. They are either physically or covalently crosslinked with each other to form hydrated polymeric networks and are also known as nanocomposite hydrogels.
They exhibit enhanced physical, chemical, electrical and biological properties compared to polymeric hydrogels. Modification of constituents in the hybrid hydrogels enables the control of release profile of contents[55].The combination of natural and synthetic material also reduces the inflammation process. Hybrid surface is known to subside the fibroblast to myofibroblast transition. Hybrid hydrogels finds its applications in sensors, actuators, drug delivery, stem cell engineering, regenerative medicine, and other biomedical devices.

Table 1: Commonly used natural and synthetic hydrogel polymers in dentistry

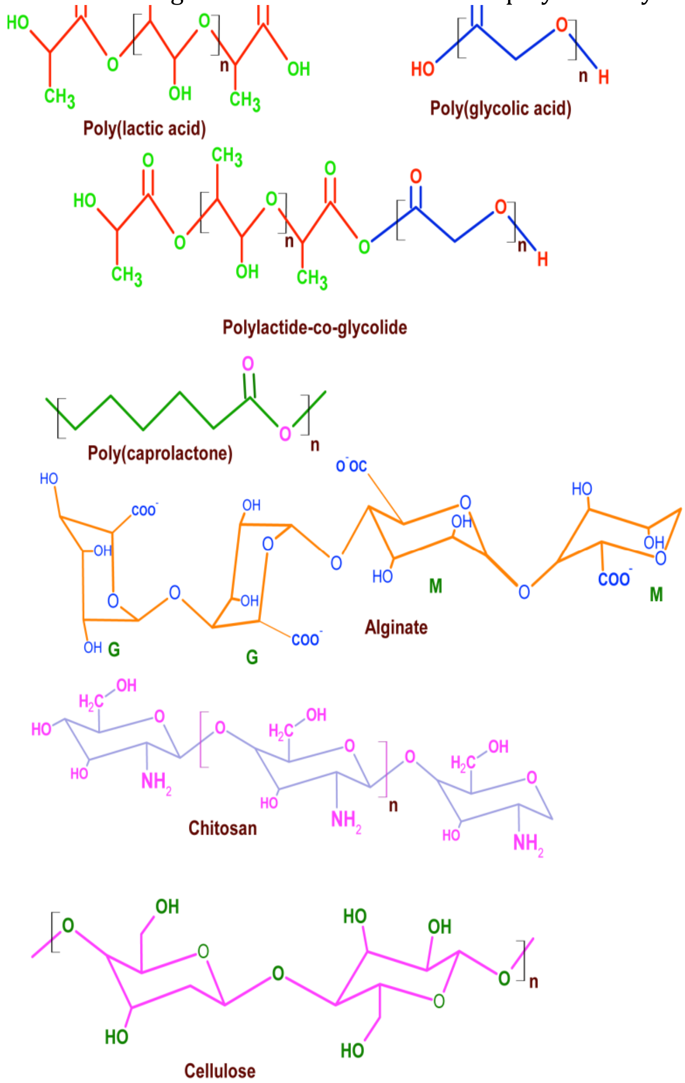
Polymeric Biomaterials	Application in dentistry
Polyglycolic acid	Dental pulp tissue engineering
Poly (lactic-co-glycolic acid)	Pulp regeneration Membrane in bone regeneration Scaffold in regenerative dentistry Drug delivery
Polyethylene glycol	Attachment of dental pulp progenitor cells
Collagen	Dental pulp proginator Vehicle to deliver cells, growth factors, anti-inflammatory molecules
Alginate	Odontoblast regeneration Tissue engineering Delivery vehicle for anti inflammatory molecules
Fibrin	pulpal regeneration Delivery vehicle for anti inflammatory molecules like IL10 and neurotrophin-3
Poly (ε-caprolactone)	Dental filling material

The most frequently used hybrid hydrogels for drug delivery and tissue engineering scaffolds includes polymeric microspheres, micelles, dendrimers, liposomes and nanogels [56,57]. The hybrid hydrogels composed of thermo-responsive chitosan-glycero phosphate hydrogel exhibits the advantages of antibacterial and osteo-inductive properties, and also is flexible in blending with other materials such as collagen and gelatin, making the composite hydrogels an attractive candidate for craniofacial bone tissue engineering. Kamoun et al., reported the synthesis of a hybrid hydrogel of N-succinyl chitosan with water-soluble dialdehyde starch via Schiff's base crosslinking reaction which are injectable and biodegradable ideally suitable for tissue engineering and cartilage repair.
Ratio between the two individual polymers of hybrid hydrogel markedly influence the physicochemical properties of resultant hybrid hydrogel.N-succinyl chitosan–dialdehyde starch hybrid hydrogels for biomedical applications [58].In adipose tissue engineering, for regeneration of adipose tissue, hybrid and multifunctional hydrogels are fabricated by incorporating decellularized adipose matrix into the hydrogels matrix recreating the adipose-like environment.

INJECTABLE HYDROGELS

Injectable hydrogels shows excellent adaptability in dentistry for minimally-invasive surgical procedures. They can be injected to the site of defect and possess the ability to conform to three-dimensional (3-D) defect upon gelling. *In situ* crosslinking injectable hydrogels have emerged as a promising biomaterial for therapeutic delivery of cells and bioactive molecules for tissue regeneration in dentistry and medicine because of their tunable tissue-like properties, controllability of degradation and release behavior. They possess all the properties of hydrogels and also supports cell infiltration. These hydrogels may be decorated with specific ECM ligands to recreate the naïve tissue environment and can deliver the bioactive molecules in specific fashion to facilitate both exogenous and endogenous cell responses towards tissue regeneration. Qiu et al., has reported in situ crosslinked, subcutaneously injectable polymer hydrogel based on poly(ethylene glycol) based copolymer containing multiple thiol (–SH) groups along the polymer backbone for protein drug delivery [59].

Figure 1: Chemical structure of polymeric hydrogels



Bakaic and co workers has reported PEG-based injectable hydrogels composed of polyethylene glycol diacrylate (PEGDA), hyaluronan (HA), and gelatin (Gn) to maintain the human dental pulp stem cell viability and facilitate cell spreading in the presence of extracellular matrix (ECM) proteins [60] .

In case of implantation of a biologically inert material, the chemical and topological features remain unrecognized by the host immune cells and mechanisms. This prevents cell-material interactions. It has been demonstrated that hydrophilic surfaces increases bioinert nature by inhibiting protein adsorption and cellular attachment. Reports also show that surface topography alteration, porosity and structure also influence inflammatory response. Porous implants are found to increase vascularization at the implant site and decrease inflammation. It has also been noted that sphere-templated porous materials enhances implant vascularization and prevents fibrosis associated with foreign body reactions. However, a complete solution for biofouling is yet to be identified. It has been cited that zwitter ionic hydrogels prepared from carboxybetaine monomer and carboxybetaine cross-linker exhibits ultra-low biofouling, minimizing foreign body capsulation around subcutaneous murine implants [61]. Heparin-releasing hydrogels incorporated with antioxidants, nitric oxides and therapeutic drugs has been applied to overcome biocompatibility-based issues. Though hydrogels are being highlighted for their biocompatibility and ECM mimicking properties the immune rejection plays a vital role in tissue regeneration or hydrogel-aided transplantation of cells. The upregulation of immunomodulation can be achieved by manipulation of material chemistry and architecture. Functionalization and induction of apoptosis of adhered FBGCs and selective tropism of anti-inflammatory cells can increases biocompatibility of hydrogel system. But major limitations for such strategies are the denaturation or bio-erosion on such coatings due to biophysical interactions between the host and material will expose the original material leading to inflammatory responses. Hence, few researches focus on altering body's innate mechanisms of immune responses [62].

More techniques like photo patterning, electro spinning and co–culture of multiple cell types are also being developed and applied towards engineering of multi–scaled and multi–layered hydrogel systems for regenerative applications

The needlessness of a second surgical intervention is the major highlight of a biodegradable implant. Hence more focus is being laid on synthetic bio-implant design and fabricationwith a controlled degradation, adjunct with an anti-inflammatory drug and a lasing functionality till the completion of therapy. Modification of the surface chemistry and surface pattern reduces the inflammatory reactions. Surface modification is also acquired by conjugation with biodegradable or a natural polymeric material bringing about change in their chemical and physical properties.

CONCLUSION

The biological polymers have excellent biomimetic features but are usually mechanically incompatible for dental applications. Synthetic polymers are mechanically robust, but their improper biodegradation and risk of inflammation are challenging. The acidic degradation products and leachable molecules are threats to dental related applications, especially in the management of dental caries because the acidity triggers cariogenic activities and may lead to secondary caries. Another issue associated with the dental biomaterials is their sterilization and the maintenance of sterility. Most sterilization techniques may alter the chemistry of the materials. Most biomaterials have an electrostatic surface, which causes the binding of small molecules from diet or from the environment through oral cavity. The difficulty in cleaning the interior networks of the dental biomaterials post implantation is also a drawback. The surgical implantation also exposes the risk of microbial invasion leading to further complications. In situ cross - linking polymers can overcome the disadvantage of the surgical implantation of the material Novel technologies to address such demerits associated with dental biomaterials are needed for the betterment of current treatment strategies.

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COMPETING INTERESTS

The authors have declared that no competing interest exists.

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