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Hydrogels – A versatile material in dentistry

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Abstract Hydrogels are a group of hydrophilic polymers which contain more than 10% of water content in their structure. They have got a specific structure and also compatibility with different condition of use. Flexibility of hydrogels, primarily due to its water content, makes it possible to use them in a myriad of applications ranging from industries to biological uses. Their application in medical field is popular due to their biocompatibility and inert nature. Hydrogels have a wide range of application in the field of dentistry also. These can be used as a better substitute for some of the materials used in dentistry. This article describes then various avenues for application of hydrogels in dentistry.

Introduction

The scope of dental treatments is increasing day by day, so is the field of dental materials. Hydrogels are a wide group of materials which has got immense use in various fields of dentistry.

A hydrogel is a three dimensional (3D) network of hydrophilic polymers. It is dimensionally stable even though it can hold a large quantities of water due to its cross-linking property of its individual polymer chains. Hydrogels were first reported by *Wichterle and Lim*(1960)(1). According to its definition, a hydrogel should contain at least 10% ofits total weight or volume of water. Hydrogels, due to its significant water content resembles natural tissue in its degree of flexibility.

Some hydrogels have been popular and widely used in dentistry viz. alginate impression material. Of late there has been a renewed interest in the development of many new hydrogels intended for various clinical procedures in dentistry.

History

The history of hydrogels dates back to 1894(2). The first material to be developed with typical properties of hydrogel was hydroxyl ethylmethacrylate(3). In 1960, *in vitro* studies were done and Buwalda *et al.* classified the hydrogel into three main blocks or three generations. The first generation mainly involves cross-linking, the second generation consists of materials capable of response to stimuli and the third generation involves stereo complex material(3).

Classification

Hydrogels are classified based on itssource, configuration, type of crosslinking,polymeric composition and physical appearance(3,4). Depending on its sources, they can be classified into synthetic andnatural hydrogels. Natural hydrogels are mainly fibrin, collagen, hyaluronic acid, chitosan, alginate, gelatine, dextran and the synthetic hydrogels are prepared from hydroxyethyl methacrylate, polyethylene glycol acrylate/methacrylate, poly (acrylamide), polyethylene glycol diacrylate/dimethacrylate, poly (vinyl alcohol), vinyl acetate, acryolic acid, methacrylic acid, N-isopropyl acrylamide, N-Vinyl-2-pyrrolidine(3,5). A third type of hydrogels is also available called combined hydrogels.

General application of Hydrogels

Owing to their structural and compatibility, hydrogels can be used widely.Flexibility of hydrocolloids, primarily due to its water content, makes it possible to use them in a myriad of applications ranging from industries to biological uses. Their application in medical field is popular due to their biocompatibility and inert nature(6).

Application of Hydrogels in medicine

Hydrogels are used in the human body as drug delivery systems, mainly in the intraocular lenses, wound dressing, surgical tissue sealant,anti-adhesive of tissue, hydrogel tissue expander, transdermal patches, and insulin delivery systems(2). These gels are used in cell encapsulation, nanoparticle coatings, and in diagnostic micro devices such as microfluidics(7–9), antibiotic drug delivery, tissue engineering(10,11) extracellular matrix, implantable devices, biosensors, separation systems, materials controlling the activity of enzymes, phospholipid bilayer destabilizing agents, materials controlling reversible cell attachment, smart micro fluids with responsive hydrogels and energy conversion systems. New designs are also available involving protein domains containing non-canonical amino acids, self-assembling peptide fibre's, artificial glycoproteins for controlling cell responses, building materials for micro chemotaxis devices, DNA recognition motifs, tunable liquid lens that permits autonomous focusing(7). They are used in growth factor delivery, carrier material for multiple tissue regeneration, injectable ceramic materials, composite for bone tissue regeneration, cell delivery for engineering complex tissues, injectable scaffold material(11). Hydrogels are also used in defibrillation electrodes, electrosurgical grounding pads, skin cushion pads, and neonatal electrodes.

Applications of hydrogels in dentistry

Hydrogels have got a wide variety of applications in dentistry. Its potential uses are described below.

a) **Application of hydrogels in Periodontology:**Guided Tissue Regeneration (GTR) is a commonly used procedure for regeneration of lost components of periodontium. It involves implantation of a biocompatible membrane around the diseased periodontium. This prevents undesirable migration of soft tissue into the defective region and provides sufficient environment and time for the regeneration of bone, cementum and periodontal ligament(3,6).The current available membranes have various limitations like being non-resorbablelike polytetrafluroetyleneand among resorbable membranes (eg.polyglycolic,polylactic acid etc) being solid and rigid which requires considerable expertise especially while correcting narrow defects.There are various promising hydrogels like Poly ethylene Glycol (PEG) hydrogel which can be used as a barrier membrane(12,13).And it has been proved that this material can be injected as a viscous solution and due to its condensation reaction, it builds a 3D network in situ. Animal studies have shown it to be biocompatible and shows aslow degradation. It alsoprevents the cell invasion by unwanted tissues. In very near future hydrogels could widely be used as barrier membranes in periodontal surgeries.

b) **Application of hydrogels in Prosthodontics:**

   a. Maxillofacial prosthetic materials:Hydrogels are colourless, odourless material. Colour can be artificially modified by pigments and colouring agents according to the hue(8–10). They are non-toxic, non-irritant, non-allergic and hence can be well supported by the host living tissue. They are bio-inert and hence do not disturb the nearby biologic tissues. They are stable in light and have optimal transilluminance and hence can be used in areas which are exposed to sunlight like the maxillofacial area. It is light in weight, flexible, and these increases the potential of it to be used as a maxillofacial prosthesis as these areas are more prone to natural creases and wrinkles as the natural appearances of external soft tissues are more important for aesthetics. The patient acceptance of this material hence can be improved(10,11,14).The rigidity of hydrogels can be altered by modifying its properties for using it in different areas of the maxillofacial region accordingly. The shelf life of the hydrogel can be extended up to 3 years by altering its physical and chemical properties and can successfully be used as the definitive maxillofacial material. It is also stable near living tissues as it permits diffusion of oxygen. Shear moduli, compressive moduli, and crosslink densities increase with increase in polyethylene glycol concentration, and the mechanical properties can also be altered by interpenetrating polymer network. This advantage can be used to improve the mechanical properties of and successfully use it as a maxillofacial material. Nano-composite gels are mainly altered hydrogels. These gels show superior mechanical properties such as increased compressive strength, tensile strength, yield stress, and this can be altered by changing or altering the crosslinking and also by reinforcing the carbon nano-tubes(15).

b. Denture adhesives: Hydrogels have a lot of desirable properties as a denture adhesive. They have various advantage compared to the conventional denture adhesive like they are zinc free and can perform in a moist environment etc. A lot of research is going on the mussel related proteins which are considered as a highly under water adhesives.

c) **Application of hydrogels in Endodontics:**Regenerative endodontics is an emerging treatment modality and it aims to replace the pulp-dentin complex (AAE position statement 2013, scope of Endodontic: Regenerative Endodontics). Tissue engineering involves the use of the triad of stem cells, scaffolds, and bioactive molecules.For regeneration of dental pulp tissue, injectable biomaterials are preferred as scaffolds.These materials allow the transport of cells into the root canal system in a minimally invasive manner. The hydrogels mimic the natural extracellular matrix materialsand hence are most preferred as scaffolds (13).

d) **Application of hydrogels in oral surgery:** Hydrogels have the potential of a wide range of application in oral surgery.They are used along with other materials in various combinations according to their compatibility. These combinations may be used efficiently inthe following conditions:

a. *Oralmucositis:*Oral mucositis, the inflammation of the oral mucosa, is a very common adverse effect after radiotherapy and chemotherapy which are the main treatment options for malignancies. It appears 2 weeks after the start of the therapy and lasts till 2–6 months after the therapy. The hydrogels combined with keratinocyte growth factors and granulocyte-macrophage colony stimulating factors promotes healing, and this can be used as a treatment modalityformucositis.

b. *Drugdelivery:*Tobramycin, a newer aminoglycoside has shown efficient results with hydrogels and this can be used against microflora during initial stages of wound healing and suppress the spread of infection locally(11). It is more effective against Streptococcus species andhencecan be used in defect areas of oral and maxillofacial regions having high chances to get infected by the oral microbiota. Sustained and targeted release are availableassmarthydrogels(14).

c. *Boneregenerationandosteo-radionecrosis:*Polylactid-co-glycolide(PLGA) microparticles are added within the injectable calcium phosphate, and this can be used for bone regeneration with controlled delivery mechanisms. These cross-linked particles use avidin to create injectable cell-containing matriceswith sufficient mechanical strength support boneregeneration(11). Osteoradionecrosis is the damage which is occurs in theirradiated bone. The main factors associated with osteoradionecrosis are hyopovasularity, hypocellularity, and hypoxia. PLGA microspheres which are packed along with the fibroblast growth factor 2 have shown to increased vascularization. This property can be applied in the treatment ofosteoradionecrosis which shows hypovascularity. Polyethylene glycol combined with de-proteinized bovine bone mineral can be used as a scaffold to maintain the bone graft volume and helps in bone regeneration(16).Polyethylene glycol is also used in target specific injection of bone marrow stem cells in the defective areas and enhances the bone growth and regeneration(17). Polyethylene glycol can be added with the arginine-glycine-aspartic acid sequence, and this can be used for extensive bone regeneration and also soft tissue integration(18). High-density nano-hydroxyapatite with the polyvinyl alcohol hydrogel has increasing biocompatibility and biologic fixation and can replace both the cartilage and bone(19).

d. *Softtissueexpansion:*Polyethylene glycol-based hydrogels are used as a soft tissue expander, and it shows high-efficiency as a soft tissue expander. Shortage of soft tissues due to resection of infected tissue may lead to poor healing. Soft tissue expansion leads to stretching of the existing skin, which stimulates and results in the formation of the new cells(15,19).

e. *Woundhealingandhemostasis*:Chitosan-based hydrogels are used as tissue adhesives as it adheres to wound site for desired period, shows good enzymatic crosslinking and anti-infective activity. This aids in wound healing and hemostasis and hence can be used postinjuries in the maxillofacial area. Few hydrogels can be altered with peptides and can be cross-linked along with thrombin and clotting factor cascade. Hyaluronic acid and gelatin show better results in woundhealing(3,11).

f. *Growthfactors:*The hydrogels can be combined with growth factors such as angiogenic growth factors, chondrogenic growth factors, and osteogenic growth factors(11). These growth factors have shown improved effects on the tissue repair, regeneration, blood vessel formation, and bone regeneration. This use of growth factors combines with hydrogels can be used for prosthesis in the defective areas in the maxillofacial areas and the growth factors will promote the regeneration of soft tissues and bone tissues around the defect without impeding the growth of the individuals(20–22).All of these combinations can be used either as an injectable material through minimally invasive methods or as a direct prosthesis in the maxillofacial area and are capable of decreasing the defect size, promoting wound healing, assisting in repair and regeneration, combating infection, minimizing the suffering caused byneoplasiaand/orotherdiseaseprocesses(23).

Conclusion

Hydrogels have wide range of applications in various fields of dentistry. There is sufficient literature available from pre-clinical and in-vitro studies regarding its potential applications. But in-vivoand clinical studies regarding the performance of these materials are yet to be reported resulting in the material being under-utilized in clinical dentistry.

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