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Biomimetic materials in pediatric dentistry- Towards future

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Abstract
With the advances in technology in dentistry, there is an active search moving toward biomimetic materials which produce a tooth-like environment rather than using artificial synthetic substances. In the early days, tooth structures were replaced by hard substances having similar strength and mechanical properties like silver amalgams, metal implants, and so on. Now using biomimicry artificially produced substances mimic the naturally found tooth structure like enamel dentine and pulpal system. Since the advent of amalgam, now till regeneration of pulp and stem cell scaffolds are used in the field of pediatric dentistry to restore the form and function of the teeth. This essay reviews the use of various biomimetic materials used in preventive, restorative, pulp capping, pulp therapy, root end closure procedures and future trends like gene therapy, pulpal stem cells, regenerative procedures, and bioengineering in pediatric dentistry.

Keywords: Biomimetic, material dentistry, pediatric dentistry

Introduction

For a very long time, biomimetics has been acknowledged as having substantial scientific and technological significance. Biomimetics is a new technology which had recently been developed for a wide range of applications in dental science. It is influenced by engineering and material science as well as pure sciences including chemistry and biology [1]. Otto Herbert Schmitt, a well-known American biophysicist, first introduced the terminology "biomimetics" in the 1950s (Julian *et al*. 2006) [2] The Greek terms "bios" and "mimesis," which mean "life" and "to imitate," respectively, are known as "biomimetics" (Bar-Cohen 2006) [3] In her book "Biomimicry: Innovation Inspired by Nature," scientist Janine Benyus defined "biomimicry" as "an innovative science that observes nature's models and previously mimics or takes inspiration from those designs and techniques to solve human challenges [4]. "This biomimicry technology is being widely applied in dentistry to create materials that are artificially identical to the natural tooth and turn them into a substance that is biocompatible. This review focuses on the biomimetic materials used in pediatric dentistry, from early developments to changing trends for a diverse range of applications.

History

Early Etruscans employed metals like gold to mimic the architecture of teeth as early as 500 BC. For dental restorations, gold was used in Egypt (2500 BC) while copper was utilized in Mesopotamia (3000 BC) [5]. Furthermore, ivory and animal bones were utilized for tooth reconstructions. Later, they restored teeth using beeswax, gums, alumina, honey, pulverized mastic, powdered pearl, and even white Corelle [8]. One of the earliest materials available for tooth repair was gold foil, which Robert Woofendale introduced to dentistry for the first time in the year 1795 [6]. The Crawcour brothers later developed the amalgam commercially available in the United States in 1833 by splitting silver from coins and adding mercury [7]. Silicate cement, the very first tooth-colored compound with a high fluoride release, was established in the late 19th century. Yet it presented pulp irritation risks, leading to the invention of direct filling methyl methacrylate resins in 1947. Despite having an excellent aesthetic appearance, these acrylic materials were unsuccessful because of polymerization shrinkage, secondary caries, postoperative sensitivity, and marginal leakage [8]. The development of bonding systems and composites in dentistry was made possible by Dr. Buonocore's discovery of acid etching in 1955 [9]. R. L. Bowen's research and trials resulted in the creation of composites in 1962, which mimic the tooth color in appearance and entirely replaced the usage of silicate and acrylic resin in cosmetic dentistry [10]. Wilson and Kent made the discovery of glass ionomer cement in 1972 after conducting an extensive study. It is made of glass particles made of fluoro aluminosilicate and polycarboxylic acid [11].

Biomimetic materials in pediatric dentistry from the past to the future

1. Glass ionomer cement (GIC)

Due to its adhesiveness to teeth, mimicking of tooth's appearance, fluoride release characteristics that make it anti-cariogenic, and most significantly due to its biocompatibility with the pulpal tissue, GIC is regarded as the first biomimetic material in pediatric dentistry. Hence the name "MAN MADE DENTINE" "DENTINE SUBSTITUTE" [12] GIC was first thought of as a replacement for amalgam but due to its weak mechanical properties, GIC reinforced with silver alloy particles (metal modified GIC) was introduced in 1977 by Williams [13]. Both the conventional GIC and metal-modified GIC showed low viscosity which led to the formation of highly viscous or condensable glass ionomer [14, 15]. Compared to standard GIC, resin-modified GIC displayed better mechanical characteristics and reduced solubility rates. But had the major disadvantage of poor biocompatibility due to the release of HEMA [16, 17]. Since the presence of the carboxylic acid group causes the ionomer cement with high solubility, polyacid-modified composite resins, also known as compomers, were developed for the treatment of dental cavities and aesthetic rehabilitation with good mechanical properties and anti-cariogenic potential [17].

2. Glass ionomer bioactive materials

- **Bioactive glass (Bag) infiltrated glass ionomer**
  In order to increase bioactivity and encourage tooth regeneration, BAG has been combined with GIC. In dentistry, the use of bioactive materials has received attention, especially for the goal of dentin remineralization. The formation of an Ap layer seems beneficial to the biocompatibility of the BAG-GICs. Due to its remineralization processes, nano BAG incorporated into GIC can be utilized as a pulp capping agent and in pulpotomy treatments [18, 19].

- **Hydroxyappatite infiltrated glass ionomer (Glass carbomer)**
  HA-infused GICs, often referred to as glass carbomers, are applied as pit and fissure sealants in pediatric dentistry due to the formation of enamel-like substances when they come in contact with the tooth [20]. The ionic interactions between polyacrylic acid and HA crystals increased its mechanical propertiesHA has bone inductive and bioactive properties hence considered a biocompatible filler material [21]. When nano HA is infused into GIC in increases the release of fluoride ions The only disadvantage is its brittle nature which can be overcome by the addition of silicone oil. Various *in-vitro* and clinical studies are needed on HA-infused GIC for its application in pediatric dentistry [21].

- **Zeolite-infused AG-GIC**
  Zeolite incorporated in Ag-reinforced GIC showed comparable mechanical characteristics to GIC with minimal water solubility and an anti-cariogenic activity against E. feacalis. It is more effective in treating teeth of persistent apical periodontitis [22].

- **Gi impregnated gutta-percha**
  The GI-impregnated Gutta-Percha (GP) cones promise to provide adhesive bonding of the active GP to intraradicular dentine and are bondable to GIC-based sealer [23].
  Hence more research for the incorporation nanoparticles like hydroxyl- (or fluoro-) apatite, titanium oxide, zirconia, and resin and combinations with GIC should be carried on which will produce a more biomimetic environment [23].

3. Calcium sulfate hemihydrate

A bone substitute that promotes tissue regeneration in dentistry is calcium sulfate, which possesses osteoconductive characteristics. This calcium sulfate breaks down into calcium and sulfate ions, which interact with phosphates in bodily fluids to generate calcium phosphate. Growth factors are also released, which promote the growth of bone at damaged locations. For direct pulp capping of primary molars with Class I cavities, calcium sulfate hemihydrate was found to be equally effective as calcium hydroxide [24].

4. Resin-based composites

- **Smart dentine replacement**
  SDR is a first-generation flowable composite material that can be filled in class I and ii cavities of primary teeth in increments of up to 4mm and exhibits low polymerization stress, low polymerization shrinkage, and high cure depth [25].

- **Self adhesive restorative composites**
  Introduced in the year 2009. These are low viscosity products recommended for minor, non-cavitating class 1 cervical lesions. However, there are very few *in vitro* reports and clinical studies that support the use of SACs as a restorative material in primary teeth; as a result, more study is required before it can be used clinically in pediatric dentistry [25].

- **Self-healing composites**
  Self-healing polymers represent a significant advance. The approach recently introduced with a urea-formaldehyde (UF) shell and disseminated in an epoxy matrix is the source of research in dental composite self-repair systems. A microcapsule's shell was shattered when the fracture front reached it, allowing DCPD to be released by capillary inside the crack plane. The vascular networks with self-healing materials that will cause the release of active healing chemicals in various situations have largely replaced the capsules. This self-healing mechanism allows for the recovery and restoration of mechanical qualities including tensile fracture strength [26].

- **Remineralizing composites**
  They are composites made from Calcium Orthophosphate (CaP) resin. The calcium and phosphate ions that promote remineralization are deposited along with the enamel HAP hydroxyapatite crystals. They are regarded as bioactive materials because, in an acidic solution, they release ions that promote remineralization [27].

- **Nanocomposites**
  Despite having a slight microleakage, the nanocomposite has been found to be a great dental material for penetrating deep pits and cracks. As a result, it can be suggested for usage as a pit and fissure sealing agent in pediatric dentistry patients [28]. When compared to traditional composite, nanocomposite showed noticeably better binding strength. Additionally, the binding strength of both types of composites was much weaker when affected dentin was present [28]

5. Calcium-enriched mixture

Calcium-enriched mixture (CEM) cement has been introduced by BioniqueDent in Tehran, Iran as a new endodontic biomaterial [29]. It is composed of silicon dioxide, phosphorous pentoxide, silicon trioxide, and calcium oxide. It has the potential to induce cementogenesis and stem cell differentiation [30]. This water-based tooth-colored cement also exhibits a superior antibacterial effect and enhanced handling properties. It is a biocompatible combination cement that releases calcium and phosphate ions to generate hydroxyapatite to encourage the construction of a dentinal bridge [31]. CEM can be effectively used in pulpotomies of primary teeth and it is economical when compared to MTA [32].

Researchers advise using CEM cement in pulp treatment methods for permanent teeth such indirect and direct pulp capping, pulpotomy, and root-end fillings because of the material's alleged benefits, potential impact on healing of the remaining pulp, and induction of dentinal bridge development [33, 34]. Although there have been few studies comparing CEM cement and MTA as dressing materials for direct pulp cap and pulpotomy in primary molar teeth, the few articles that have been published have found that these biomaterials are appropriate for the treatment [35]. Clinical and radiological results demonstrated that vital pulp therapy utilising calcium-enriched mixture (CEM) cement can successfully treat primary molars with permanent pulpitis [36].

- **Cem pulpotomy**

  CEM pulpotomy uses a bioregenerative material that is biocompatible, is faster and simpler (which is advantageous when treating children), and does not require canal access. The only significant danger associated with this unique technology is the use of NaOCl irrigation, which is reduced by efficient isolation, high vacuum evacuation, controlled irrigation, and efficient child management [37].

  Recent randomized clinical trials show that direct pulp capping and pulpotomy of primary molar teeth with CEM cement result in effective treatment outcomes [38]. Additionally, a recent examination of a primary molar pulpotomy using CEM cement using cone beam computed tomography and histology revealed complete tubular dentin bridge development for the first time beneath the biomaterial [39].

6. Calcium hydroxide

Hermann introduced Calcium Hydroxide to dentistry in 1928. The mineralizing and antibacterial properties of calcium hydroxide have long been known. Depending on the existing odontoblasts reactionary or reparative formation occurs [40].

However, because it frequently causes the development of chronic pulpal inflammation and internal root resorption, the use of calcium hydroxide is not typically advised for primary dentition [41].

7. Bioceramics

- **Mineral trioxide aggregate**

Only the MTA seems to have specific qualities as to be considered as an appropriate material: its biocompatibility, its ability to harden in a humid environment, and its sealing properties. As of today, there is no scientific evidence that makes clear which is the most appropriate material to be used in deciduous teeth pulpotomy [43].

Besides primary teeth pulpotomy, MTA is used for various applications like permanent and primary pulp capping, repair material for perforations, apical closure material as in apexification of necrotic immature permanent teeth, and apexogenesis of immature vital teeth [44].

- **Biodentine**

  Due to MTA's shortcomings, such as its lack of affordability, extended setting time, challenging handling characteristics, and discoloration features, septodont produced "BIODENTINE," which demonstrated superior biocompatibility as well as better mechanical and sealing properties with dentine. Due to its biocompatibility, bioactive nature, and good physical and mechanical qualities, this substance—known as "Bioactive Dentine Substitute" or "Dentine In Capsule"—is regarded as an ideal restorative material [45, 46]. By producing TGF-BETA, it has the capacity to trigger pulpal cells to start early mineralization, promoting pulp repair [47]. Biodentine was employed in a study by Nowicka *et al*. as a pulp capping material, and it was discovered that it showed dentine bridge production without any inflammatory response. One of the main benefits of utilizing biodentine in pulpotomy is that it is less time-consuming and serves as both a filling and a dressing material at the same time. Also used in apex closure and root repair procedures [48]

- **Theracal LC**

  TheraCal LC is a fourth sgeneration calcium silicate material that has been enhanced with light-curable resin. It is a single paste calcium silicate-based substance that the manufacturer recommends be used as a protective liner for use with restorative materials, cement, or other base materials, as well as a pulp capping agent, pulpotomy [49].

8. Stem cells in pediatric dentistry

When employed in paediatric patients, stem cells have the ability to promote apexogenesis and revascularization. The DPSCs and SCAPs should ideally endure endodontic therapy so as to support apexogenesis. The SCAPs are stimulated by Hertwig's epithelial root sheath to create fresh dentine deposits and the remaining apical tissue. Perivascular tissues, areas near blood arteries, and peripheral nerve ends are possible sites for DPSC niches. Many studies are going on dental stem cells for its use in practice [50].

9. Future dental applications of bioengineering with stem cell

The creation of scaffolds and other support structures to house the cells and growth factors is a crucial step in bioengineering. In this new era of restorative dentistry, research has advanced significantly in terms of leveraging the biological activity of oral tissues to speed wound healing and tissue regeneration. The nature, potential, and behaviour of dental stem/progenitor cells are currently very little understood. However, there are a tonne of prospects for their use in dental tissue regeneration, which will have a big impact on how dental disease is treated [50].

Conclusion

The introduction of biomimetics into dental science has made remarkable applications in preventive, restorative, and endodontic procedures in pediatric dentistry to be used as a fissure sealant, cavity liners, bases, restoration material, obturation material, pulp capping, pulpotomy agents which produce a natural tooth like environment thus making it more biocompatible

We declare that this manuscript is original, has not been published before, and is not currently being considered for publication elsewhere.

Authors contribution

The authors confirm their contribution to the paper as follows: Study conception and Design, data collection, analysis and interpretation of results, and draft manuscript preparation by Rajeshwari Baskar and Daya Srinivasan.

All authors reviewed the results and approved the final version of the manuscript.

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