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RESEARCH ARTICLE

CONQUERING NEWER HORIZONS OF RESTORATIVE DENTISTRY WITH BIOMIMETIC MATERIALS: A COMPREHENSIVE REVIEW

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Abstract

With the arrival of advanced technology, numerous changes have been made in the field of restorative dentistry in the last few decades. Biomimetic materials, with their biocompatible nature and excellent physicochemical properties, have demonstrated the ability to prevail over some of the significant limitations of previous generation materials. They can function as long-lasting esthetic and restorative materials, cements, root repair materials, root canal sealers, filling and regenerative materials which have superior biocompatibility, high strength, sealing ability and antibacterial properties when compared to other parallel materials. Hence, their application has become indispensable. This essay reviews the various biomimetic materials available from the past to the future and their biological properties in the field of paediatric restorative dentistry and endodontics.

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Introduction:-

From the dawn of history, dental practitioners have been on the quest for ideal restorative dental materials and nothing surpasses biomimetic materials in this regard. The term “bio” means life and “mimesis” in Greek means to imitate. Biomimetics is defined as the study of the structure, formation, and function of biologically produced substances and materials and biological mechanisms and processes, especially for the purpose of synthesizing similar products by the means of artificial mechanisms which mimic natural ones. A material fabricated by the biomimetic technique based on natural processes found in biological systems is said to be a Biomimetic material. (1)

The main principle of Biomimetic Dentistry is to replace lost dental tissues with artificial and naturally available materials to restore their full function that can withstand all functional stresses along with the maintenance of aesthetic results. It goes by various names Bionics, Biognosis, etc. (2) Even though the concept is ancient but the execution is gathering momentum only recently which could be due to the increased need for congenial technology and also the availability of advanced techniques. This essay will walk us through the earliest to the most recent biomimetic materials available in the paediatric dental world.

Various Biomimetic materials available are:

Glass Ionomer Cement (GIC)

Glass ionomer cement is considered one of the most commonly used biomimetic materials for minimally invasive dentistry. It falls under the umbrella of Biomimetic Restorative Dentistry because it has mechanical properties similar to dentin, adhesiveness to tooth structures, and its fluoride-releasing property thus attributing to its multifactorial usage. Their fluoride-releasing capacity has bactericidal properties and stimulates sclerotic dentin formation which is one of their outstanding properties amongst many others. (3)(4)

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Fig1:- Restorative GIC.

In dentin replacement, GIC recreates dentin's functional strength and rejuvenates the remaining affected dentin through remineralization. It has been referred to as **"MAN MADE DENTIN"** and **"DENTIN SUBSTITUTE"** because of the extensive use of this cement as a dentin replacement material. However, it should only be used as a final restorative material in low-stress areas, and must be secured by resin composite in high-stress areas owing to its poor mechanical properties. As a biomimetic dentin substitute, glass ionomers when used as a base prior to the placement of composite resin (Direct Sandwich Technique) facilitate the reduction in the number of shrinkage stresses that occur between the cavity preparation walls and direct resin restoration by approximately 20% to 50%.(5)

Clinical applications:

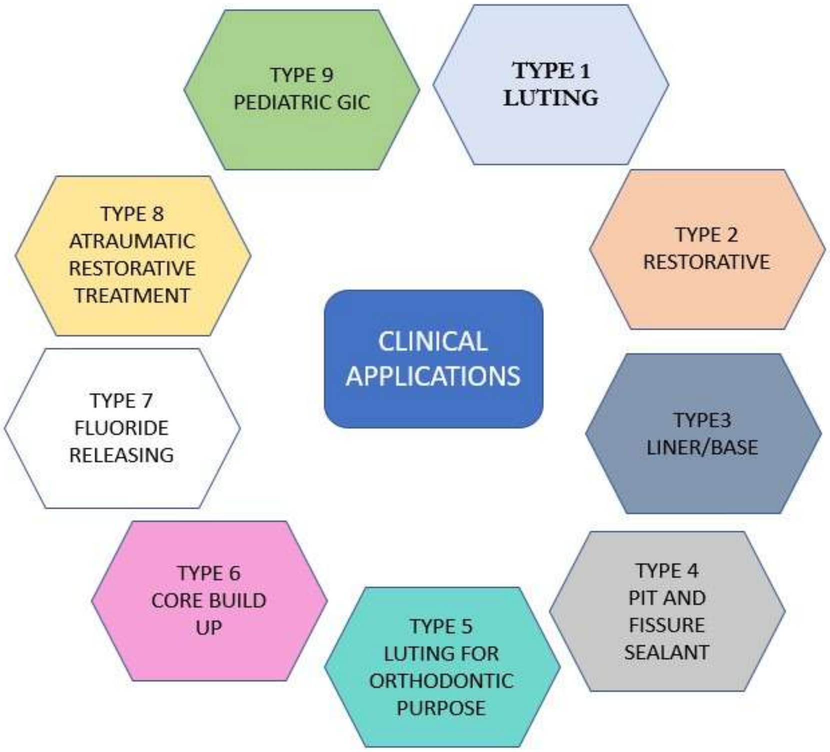


Fig 2:- Clinical applications of GIC.

Recent advances:

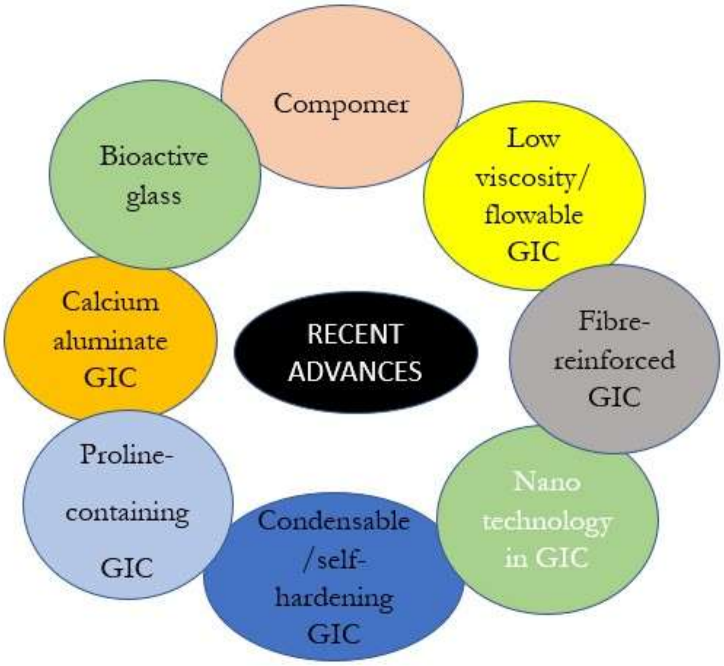


Fig 3:- Recent advances of GIC.

Bio-Active Glass (BAG)

A material is reputed to be bioactive when the engineered substance produces a physiologically active response by forming a strong material tissue bond when it interacts with the biological system. The development of bioactive glasses (BAGs) is a milestone in itself because of their biocompatible mechanical properties. The working mechanics of BAG is mimicking the natural hard tissue composition and has a bioactive role in the field of regeneration. The Bioactive property of BAG is governed by the following factors:

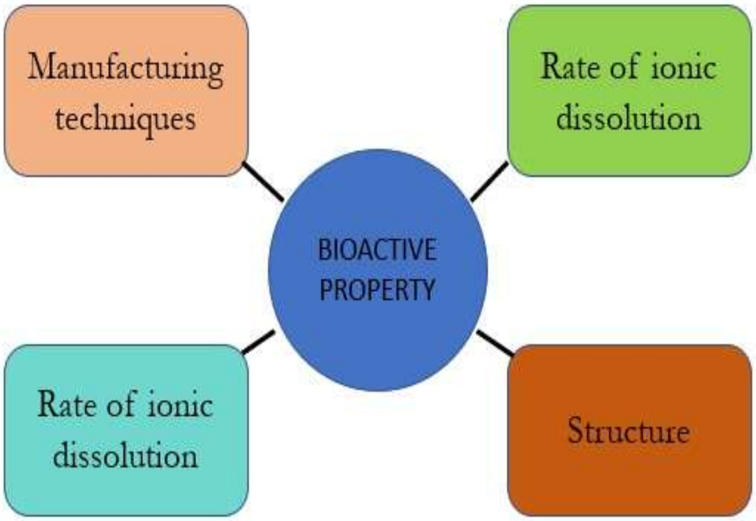


Fig 4:- Factors governing bioactive property of BAG.

Resin composites with BAG and fluoride-releasing capacity eliminate enzymatic degradation at the dentin interface and enhance dentin remineralization. Bioactive glasses have various utilities including dental restorative materials, toothpaste, mineralizing agents, desensitizing agents, pulp capping, root canal treatment, and air abrasion. (11)(12)(13)

Fig 5:- Bioactive Glass.

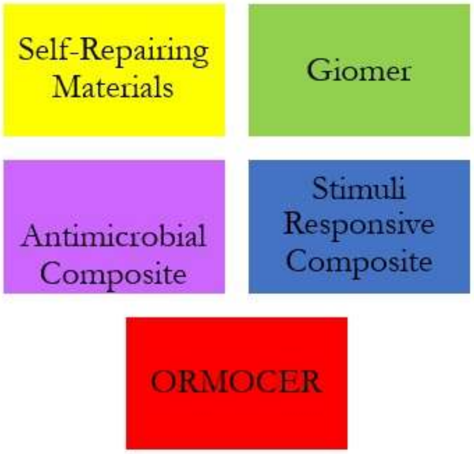
Resin-Based Composites

Modern dental composite restorative materials began in the early 1960s, with the discovery of Bowen‟ s Bis-GMA (2,2-bis [4-(2-hydroxy-3 methacryloxypropoxy) phenyl]- propane) with inorganic particle formulations. Dental composites are composed of inorganic fillers, synthetic polymers, initiators, and activators that promote light-activated polymerization of the organic matrix to facilitate the formation of cross-linked polymer networks, and silane coupling agents that bond the reinforcing fillers to the polymer matrix. Composite resins are considered superior to amalgam on the ground of their physical properties and the longevity of the material. The technique involves minimal preparation decreasing the chances of pulpal insults and their respective involvement while working on the principle of conservation. Therefore, it preserves tooth vitality and structure, minimizing the possibility of fracture. (6)

Fig 6:- Composite material.

Fig 7:- Pre- and post-Composite Restorations.

Recent advances:



Self-Repairing Materials

Giomer

Antimicrobial Composite

Stimuli Responsive Composite

ORMOCER

Fig 8:- Recent advances of Resin-Based Composites.

Smart Dentin Replacement (SDR)

SDR is the first flowable posterior composite material for dentin replacement and is considered one of the most exciting technological advancements in dentistry toward technique simplification. It can be bulk-filled in increments of up to 4mm in class 1 and 2 cavities. A polymerization modulator is chemically embedded in the backbone of polymerizable resin and hence it is based on "**Stress Decreasing Resin Technology".** It is considered superior to other parallel filling techniques as it has the following characteristic features:

Low polymerise stress & shrinkage

Time saving

Ease of application

Enhanced translucency facilities adequate curing efficiency

Self levelling consistency for optimum cavity wall adaptation

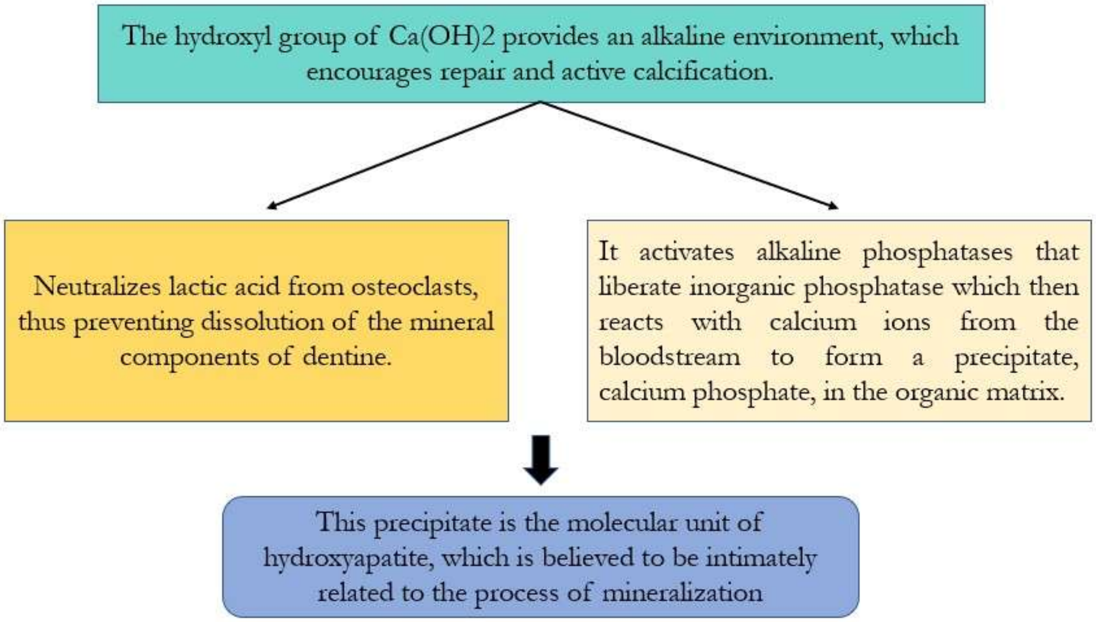
Fig 9:- Characteristic features of SDR.

Calcium Based Materials

Calcium Hydroxide

Calcium hydroxide was introduced by Herman in dentistry in 1990. It has been included in several materials and antimicrobial formulations that are used in various treatment modalities. When used as a pulp-capping agent and in apexification cases, a calcified barrier may be induced by calcium hydroxide

Biological action(7)



The hydroxyl group of Ca(OH)2 provides an alkaline environment, which encourages repair and active calcification.

Neutralizes lactic acid from osteoclasts, thus preventing dissolution of the mineral components of dentine.

It activates alkaline phosphatases that liberate inorganic phosphatase which then reacts with calcium ions from the bloodstream to form a precipitate, calcium phosphate, in the organic matrix.

This precipitate is the molecular unit of hydroxyapatite, which is believed to be intimately related to the process of mineralization

Fig 10:- Biological action of Calcium Hydroxide.

Fig 11:- Calcium hydroxide.

Applications in pediatric dentistry

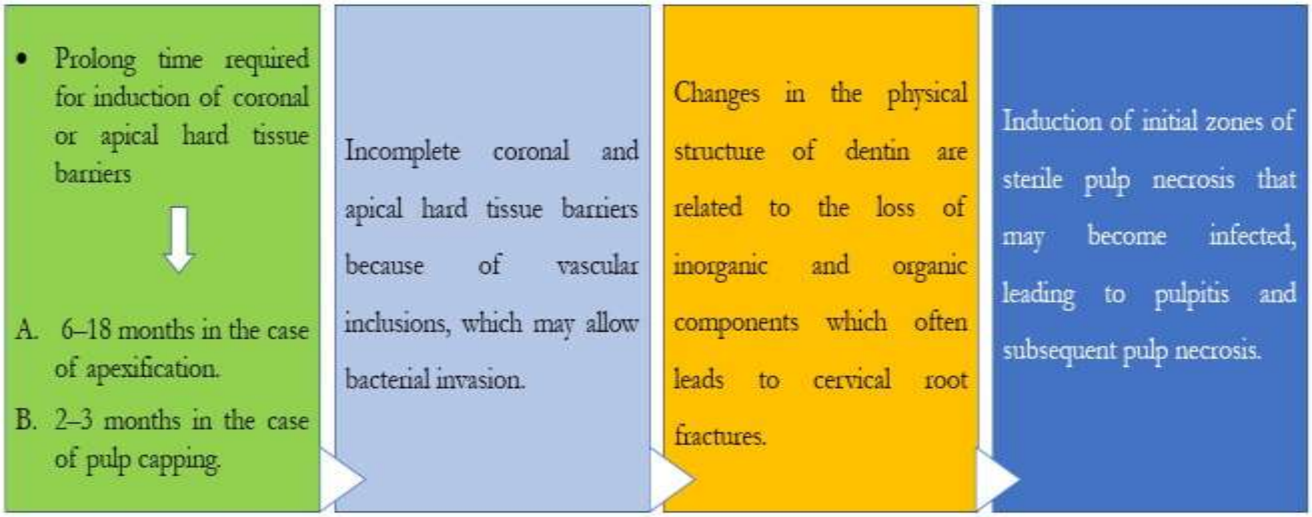
Pulp capping agent

Pulpotomy agent

Apexification

Fig 12:- Applications of Calcium Hydroxide.

Limitations of calcium hydroxide



- Prolong time required for induction of coronal or apical hard tissue barriers

⇩

A. 6–18 months in the case of apexification.

B. 2–3 months in the case of pulp capping.

Incomplete coronal and apical hard tissue barriers because of vascular inclusions, which may allow bacterial invasion.

Changes in the physical structure of dentin are related to the loss of inorganic and organic components which often leads to cervical root fractures.

Induction of initial zones of sterile pulp necrosis that may become infected, leading to pulpitis and subsequent pulp necrosis.

Fig 13:- Limitations of Calcium Hydroxide.

Calcium Sulphate (CS)

Calcium sulphate (CS) is an inorganic compound that is commercially popular as gypsum plaster or plaster of Paris. It is a ubiquitous compound that has been incorporated into several dental and medical procedures. It has been shown to be completely bioabsorbable, osteoconductive, allows fibroblast migration, does not cause an inflammatory response and does not elevate serum calcium levels. Primarily, it was used to help treat a variety of osseous defects by acting as a bone substitute Whilst the outcomes of these applications are varied, they have shown to be beneficial within the disciplines of periodontics, endodontics, and oral & maxillofacial surgery and hence can be used in the following ways:

Fig 14:- Clinical applications of Calcium Sulphate.

Calcium Phosphate (CP)

Calcium phosphate materials have received a lot of research attention in recent years because of their chemical similarity to teeth and bone. They are attractive biomedical materials owing to their excellent biocompatibility and nontoxicity of their chemical components. The first calcium phosphate materials were used in the 1920s which were used as bone substitutes or grafts. With the advancement of current technology, it can be used in the following ways:

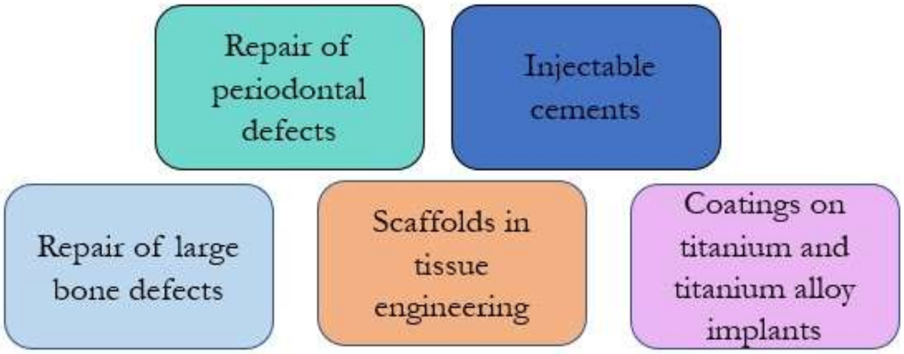
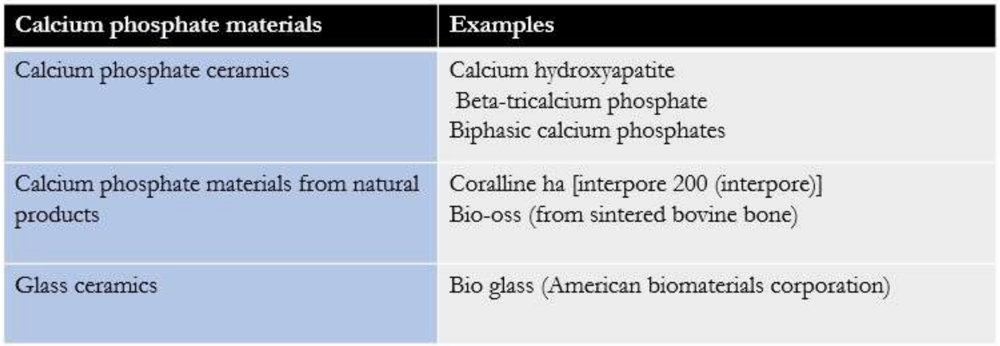


Fig 15:- Clinical applications of Calcium phosphate.

The following are examples of calcium phosphate materials:



Calcium phosphate materials	Examples
Calcium phosphate ceramics	Calcium hydroxyapatite Beta-tricalcium phosphate Biphasic calcium phosphates
Calcium phosphate materials from natural products	Coralline ha [interpore 200 (interpore)] Bio-oss (from sintered bovine bone)
Glass ceramics	Bio glass (American biomaterials corporation)

Fig 16:- Calcium Phosphate materials and their respective examples.

Calcium Enriched Mixture (CEM)

It has been recently introduced as a hydrophilic alkaline tooth-colored cement (pH~11) that releases calcium hydroxide (CH) during and after setting. The major elements of this cement powder are calcium oxide, calcium sulphate, phosphorus oxide, and silica. CEM has favourable physical properties that include their film thickness, flow and primary setting time. This cement is biocompatible and induces the formation of cementum, dentin, bone and periodontal tissues. This novel material has an antibacterial effect comparable to Calcium hydroxide and superior to MTA and sealing ability similar to MTA. Clinical applications of CEM include:

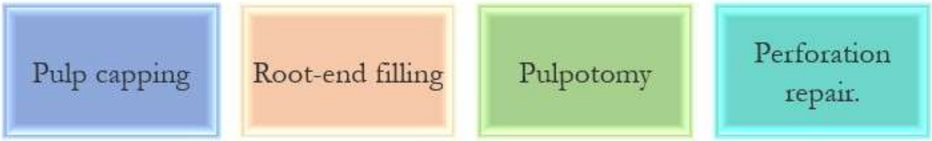


Fig 17:- Clinical applications of CEM.

Endosequence Root Repair Material (Errm) Putty, Errm Pasterrm Putty Fast Set (Fs) And Iroot FS

Endosequence root repair materials are delivered as a premixed mouldable putty or as a preloaded paste in a syringe with delivery tips used for intracanal placement. It is composed of calcium phosphate monobasic, zirconium oxide, calcium silicates, and tantalum oxide. ERRM forms tag-like structures inside the dentinal tubules that allow gingival fibroblasts to grow on their surface. RRMs are premixed, single-component materials that can be directly used from the syringe and do not require mixing, thus differentiating them from MTA, bioaggregate and biodentine.

Mineral Trioxide Aggregate (MTA)

MTA is potentially one of the most versatile materials of this century in the field of dentistry. It is a bioactive material, which was introduced by Mahmoud Torabinejad at Loma Linda University, California, USA, and was first described in the dental scientific literature in 1993. Studies on MTA reveal that it not only exhibits good sealing ability, relative ease of manipulation, good biocompatibility, and excellent long-term prognosis but also favourstissue regeneration. MTA was developed and recommended for endodontic procedures because it has the following outstanding properties: (6)(7)

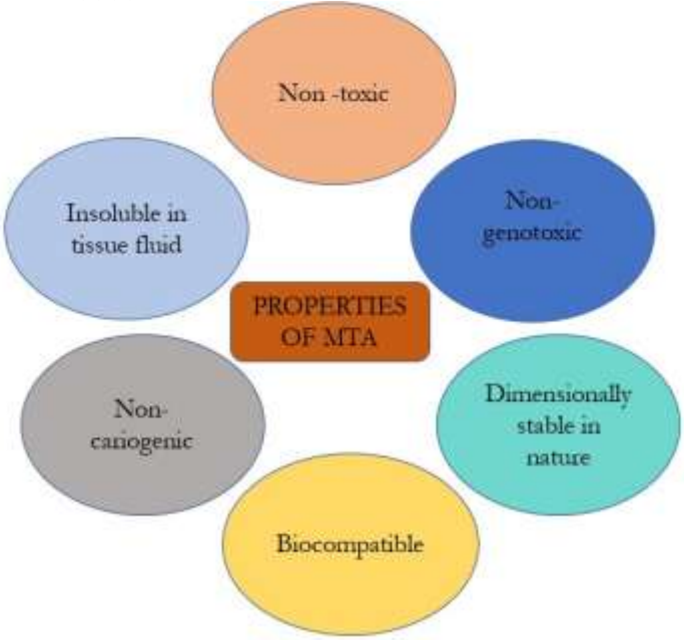


Fig 18:- Properties of MTA.

Fig 19:- Pro Root MTA.

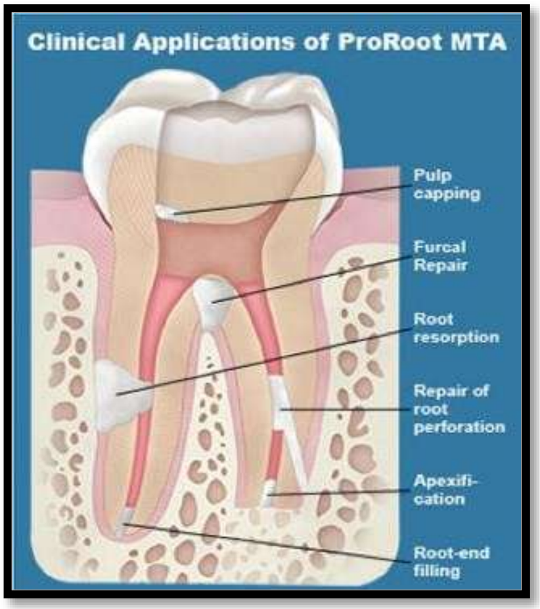


Fig 20:- Clinical applications of MTA.

Biological Action of MTA

The mechanism of action of MTA is very similar to the effect of Calcium Hydroxide. According to Parirokh and Torabinejad et al. when MTA is placed in direct contact with human tissues, the material does the following (8)

- Forms Calcium hydroxide that releases calcium ions for cell attachment and proliferation
- Creates an antibacterial environment by its alkaline pH
- Modulates cytokine production
- Encourages differentiation and migration of hard tissue-producing cells
- Forms Hydroxyapatite on the MTA surface and provides a biological seal

Fig 21:- Biological actions of MTA.

Clinical applications of MTA in primary teeth

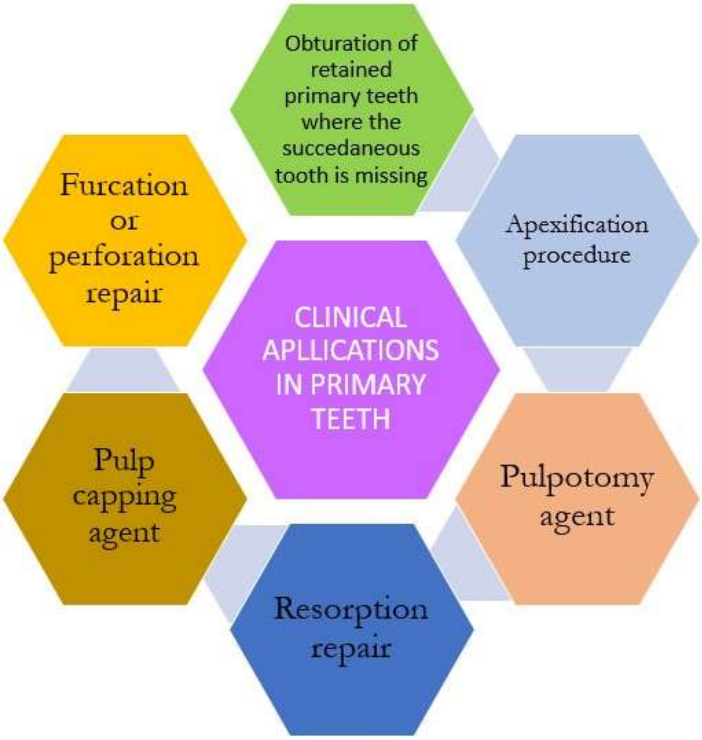


Fig 22:- Clinical applications of MTA in primary teeth.

Clinical applications of MTA in permanent teeth:

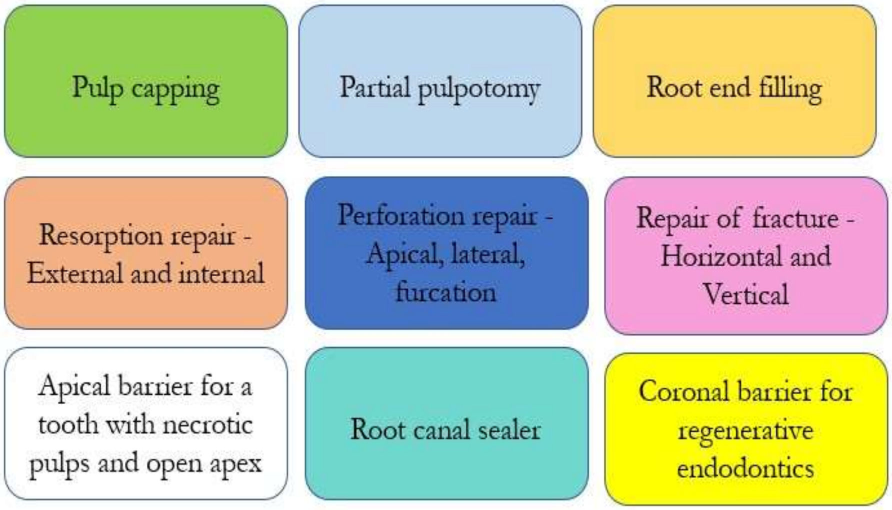


Fig 23:- Clinical applications of MTA in permanent teeth.

Limitations

The drawbacks of MTA include its discoloration potential, long setting time, difficult handling characteristics, presence of toxic elements in the material composition, an absence of a known solvent for this material, and lastly the high material cost.

Biodentine

It is relatively a newer calcium silicate-based material introduced in 2010 by Gilles and Olivier. It is a dentin substitute that can be used as a coronal restorative material and can also be placed directly in contact with the pulp.

Their fast-setting property allows them to become intraorallyfunctional immediately after placement and also allows immediate crown restoration. (9)

Biological Action

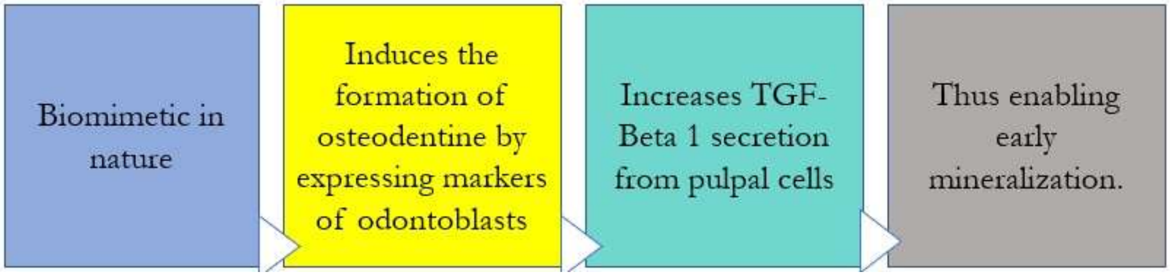


Fig 24:- Biological action of Biodentine.

Biodentine is capable of inducing the apposition of reactionary dentine by odontoblast stimulation and reparative dentin formation via cell differentiation. Its high alkalinity property has inhibitory effects on microorganisms. (10)

Fig 25:-Biodentin

Applications in Pediatric Dentistry

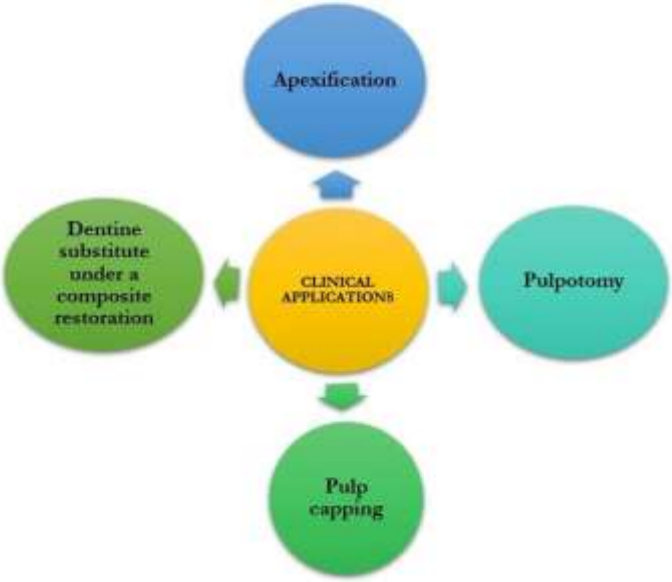


Fig 26:- Clinical applications of Biodentine.

Bio- Aggregate

BioAggregate (BA) also referred to as DiaRoot (DiaDent) BioAggregate (Innovative Bioceramix, Vancouver, BC, Canada) is a material that was introduced for root-end filling, perforation repair, as well as pulp capping in 2006. It is a material with bioactivity, certain antibacterial properties, fine particle size, along with no reported toxicity. Their aluminium-free formulation stimulates the proliferation of human PDL fibroblasts and also assists in periodontal regeneration. However, numerous in vivo and evidence-based investigations are required in order to determine the material's efficacy in clinical applications as by far all investigations have been laboratory-based studies. (6)

Fig 27:- BioAggregate material.

Bioceramic Materials

Endosequence Bc Sealer

It is a revolutionary premixed endodontic sealer utilizing new bioceramic nanotechnology. Unlike traditional sealers, their nanoparticle size allows it to flow readily into canal irregularities including the dentinal tubules. It is a highly radiopaque and hydrophilic sealer that has absolutely no shrinkage and chemically bonds to both dentin and bio-ceramic gutta-percha. It makes use of the moisture naturally present in dentin to initiate and complete its setting and its high alkaline pH imparts anti-bacterial properties. (3)

Bioceramic Gutta-Percha

These are Gutta-Percha cones impregnated and coated with bioceramic nanoparticles and are verified with laser for tip and taper accuracy which allows "three-dimensional" bonded obturation to overcome the limitations of conventional obturation.

Remineralizing Agents

Casein Phosphopeptide Amorphous Calcium Phosphate (CPP-ACP):

The subsurface carious lesions can be remineralized through the diffusion of calcium and phosphate ions into the tooth structure. Casein is the predominant phosphoprotein found in bovine milk that has organoleptic properties. CPP stabilizes calcium and phosphate in the solution state and thus making it a calcium and phosphate reservoir. The incorporation of the CPP-ACP nanoparticles into the cross-linked matrix of the GIC increases the following properties.

Fig 28:- Properties of GIC enhanced by CPP-ACP.

Tooth Mousse™ (Europe and Australasia) or MI Paste™ (USA and Japan) has 10% w/w CPP-ACP nanocomplexes. (6)

Demineralized Dentin (DDM):

The dentin matrix which is used for implant biomaterial has both osteogenic and chemotactic potential. Demineralized bone matrix induces chondrogenesis and osteogenesis when it comes in contact with mesenchymal cells.

Enamel Matrix Derivative (EMD):

It is derived from pig enamel matrix (Emdogain; Straumann AG, Basel, Switzerland) and has been employed to restore functional periodontal ligament, cementum and alveolar bone in patients with severe attachment loss through recruitment of cementoblasts onto the root surface.

Regenerative Endodontics And Tissue Engineering

Dental regeneration is a process in humans by which specialized dental tissues are replaced by the recruitment, proliferation, migration, and differentiation of dental stem cells. Stem cells, scaffolds, and growth factors are considered 3 key elements used for tissue regeneration

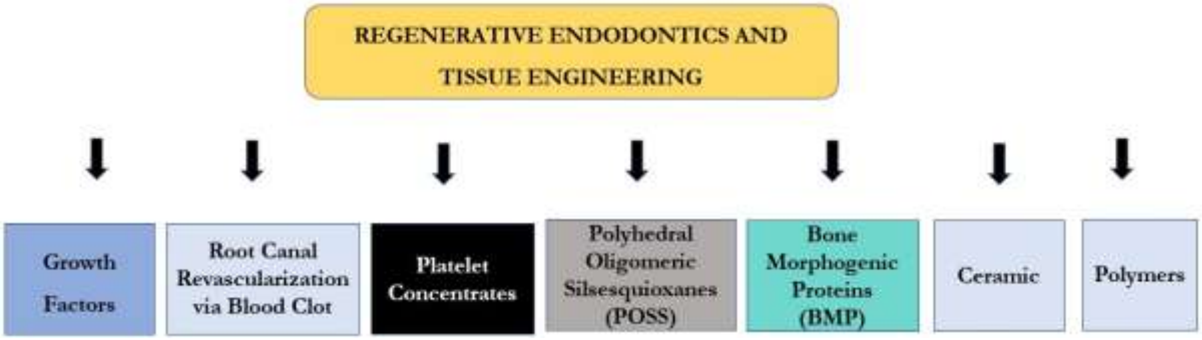


Fig 29:- Materials used for Regenerative endodontics and tissue engineering

Growth Factors

Growth factors are considered engines that drive the wound healing process. (6) Following are the examples of varied growth factors:

Platelet derived growth factor	It plays a key role in the chemotaxis of neutrophils that acts with other growth factors to produce collagen.
Keratinocyte growth factor	KGF through keratinocyte differentiation plays a vital role in wound re-epithelialization.
Transforming growth factor	TGF induces extracellular matrix deposition and collagen formation.
Fibroblast growth factor (FGF)	FGF plays role in fibroblast proliferation, angiogenesis, and matrix deposition.
Vascular endothelial growth factor	VEGF increases vascular permeability at the capillary level.
Epidermal growth factors (EGF)	EGF act in an autocrine fashion. It plays an important role in extracellular matrix mineralization, a complex process required for proper bone regeneration,
Recombinant TGF-b3	It can be used as a growth factor enhancer for all surgically created wounds.

Fig 30:- Growth factors and its functions.

Root Canal Revascularization Via Blood Clot

When Root canal revascularization is performed via blood clot in the apical region, the bioceramic material is placed as a mid-root/coronal plug, thereby providing a permanent and superior quality seal. Jung et al. reported that by activation of MAPK pathway bioaggregate, biodentine, and MTA causes odontoblastic differentiation and mineralization.

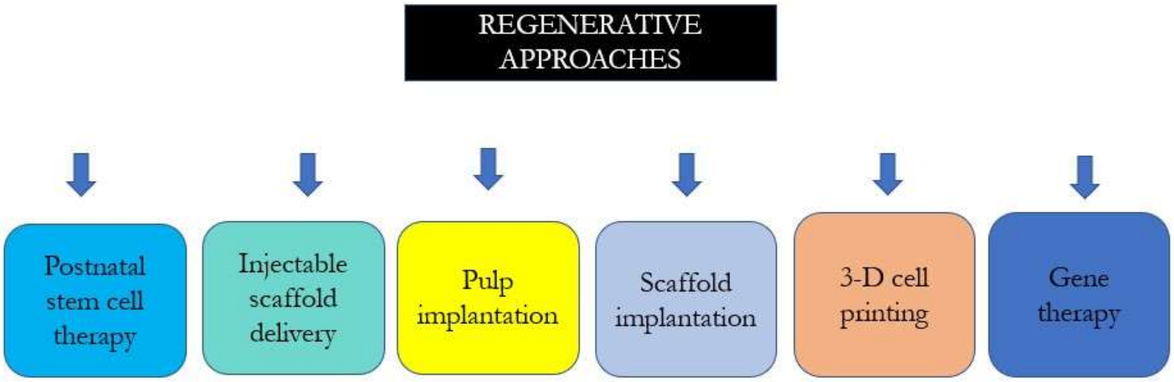


Fig 31:- Regenerative approaches.

Platelet Concentrates

It was first described by Whitman et al. Platelet-rich plasma (PRP) is generated by differential centrifugation and serves as a reservoir of critical growth factors that regulate wound healing.

Fig 32:- Growth Factors.

PRP requires biochemical blood handling with the addition of anticoagulants while platelet-rich fibrin (PRF) does not require anticoagulants. A second-generation platelet concentrate, Leucocyte and platelet-rich fibrin (L-PRF) was developed by Choukroun et al in France that does not contain any anticoagulant agents.

Polyhedral Oligomeric Silsesquioxanes (POSS)

Biomaterials such as polyhedral oligomeric silsesquioxanes (POSS) and polyhedral oligomeric silicates (POS) may be prepared by the incorporation of POSS molecules in order to provide a nanoscopic topology that favors bioavailability, differentiation and cellular modulation. The advent of POSS has led to the formulation of composites and dental adhesives with ameliorated mechanical and physical properties.

Bone Morphogenic Proteins (BMP)

BMP plays a key role in dental bone grafting and implant placement, fracture healing and spinal fusion. It is advantageous in patients with known risk factors as BMP-2 and BMP-7 are superior to autologous bone grafting. Additionally, it has the following properties of interest:

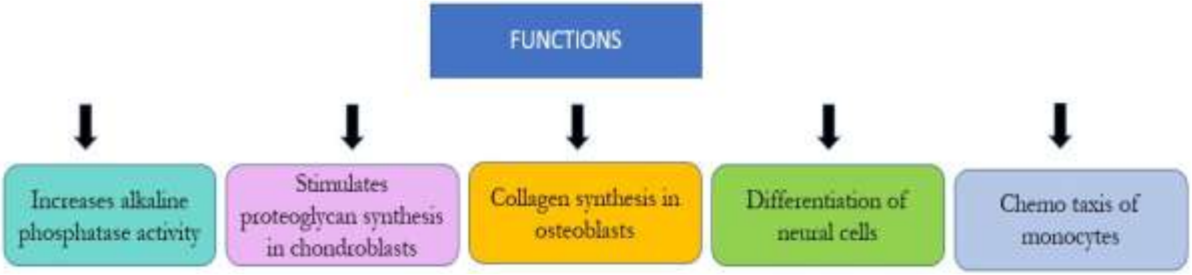


Fig 33:- Functions of Bone Morphogenic Proteins.

Ceramic

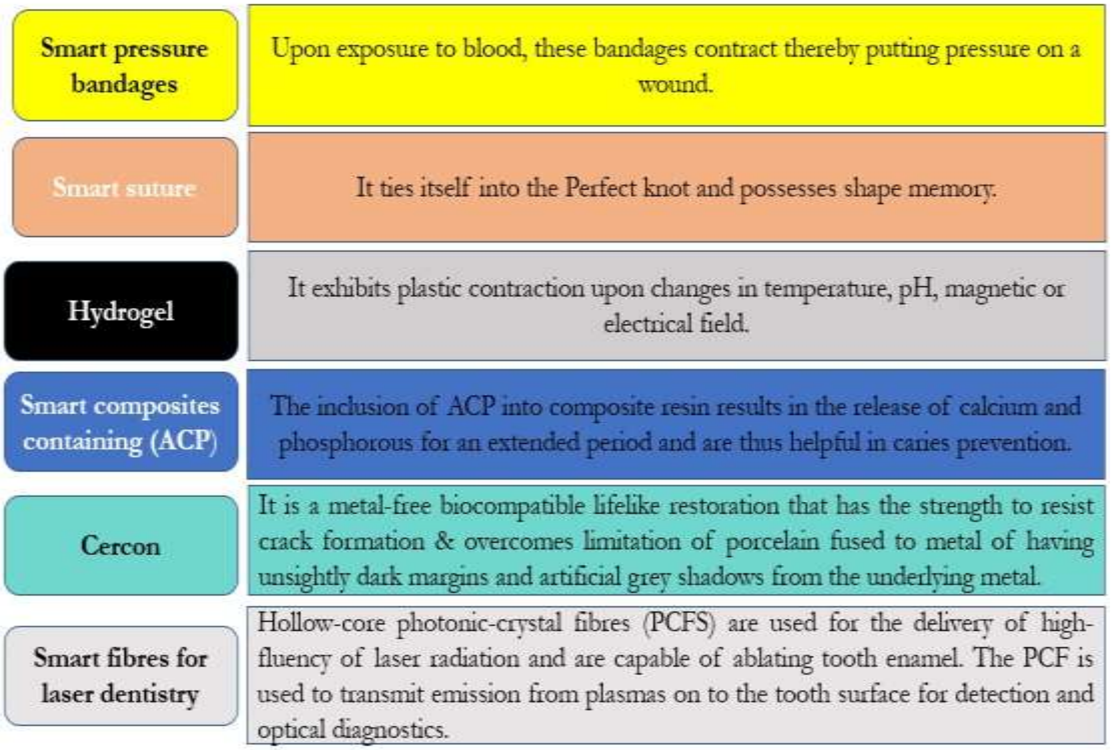
Ceramics are being examined for bone tissue engineering and along with dental applications. Hydroxyapatite (HA), a major inorganic component of bone is a calcium phosphate-based ceramic. Novel ceramic bone replacement material Ceraball, may act as a carrier for pluripotent mesenchymal stem cells, bone marrow and stromal cells.

Polymers

Polymers like polymethylmethacrylate (PMMA), polyethylene (PE), and polyurethanes have been used in dental surgery for decades. Polyglycolic acid (PGA), polylactide (PLA), and polydioxanone (PDS) are primarily used as suture materials or as resorbable bone fixation devices. Fibrin glue is used as a tissue adhesive to enhance surgical wound repair.

Smart Materials

It is defined as the class of materials that are highly responsive and poses the inherent capability to sense and react according to changes in the environment. They can be classified as passive and active smart materials. Passive smart materials respond to external change without any external control, while active smart materials utilize a feedback loop that allows them to function like a cognitive response through an actuator circuit. Various smart materials that are currently used are as follows:



Smart pressure bandages	Upon exposure to blood, these bandages contract thereby putting pressure on a wound.
Smart suture	It ties itself into the Perfect knot and possesses shape memory.
Hydrogel	It exhibits plastic contraction upon changes in temperature, pH, magnetic or electrical field.
Smart composites containing (ACP)	The inclusion of ACP into composite resin results in the release of calcium and phosphorous for an extended period and are thus helpful in caries prevention.
Cercon	It is a metal-free biocompatible lifelike restoration that has the strength to resist crack formation & overcomes limitation of porcelain fused to metal of having unsightly dark margins and artificial grey shadows from the underlying metal.
Smart fibres for laser dentistry	Hollow-core photonic-crystal fibres (PCFS) are used for the delivery of high-fluency of laser radiation and are capable of ablating tooth enamel. The PCF is used to transmit emission from plasmas on to the tooth surface for detection and optical diagnostics.

Fig 34:- Smart Materials.

Conclusion:-

Biomimetic dentistry would successfully replace lost dentin, enamel, cementum, and pulp and open a new era of dentistry. Biomimetic materials have outstanding properties that comprise features like antibacterial properties, regenerative properties, enhanced biocompatibility, superior sealing ability, and strengthening of the root following obturation and hence they can function as a root canal sealer, regenerative materials, filling materials, cements and root and crown repair materials. Contemporary biomaterials have shown the ability to prevail over the limitations of traditional materials. However, like any material there exist limitations when considering criteria for categorizing them as ideal materials. Several in vitro and in vivo studies have demonstrated good results, but randomized and double-blind studies of sufficient duration with biomimetic materials are required to confirm long-term success.

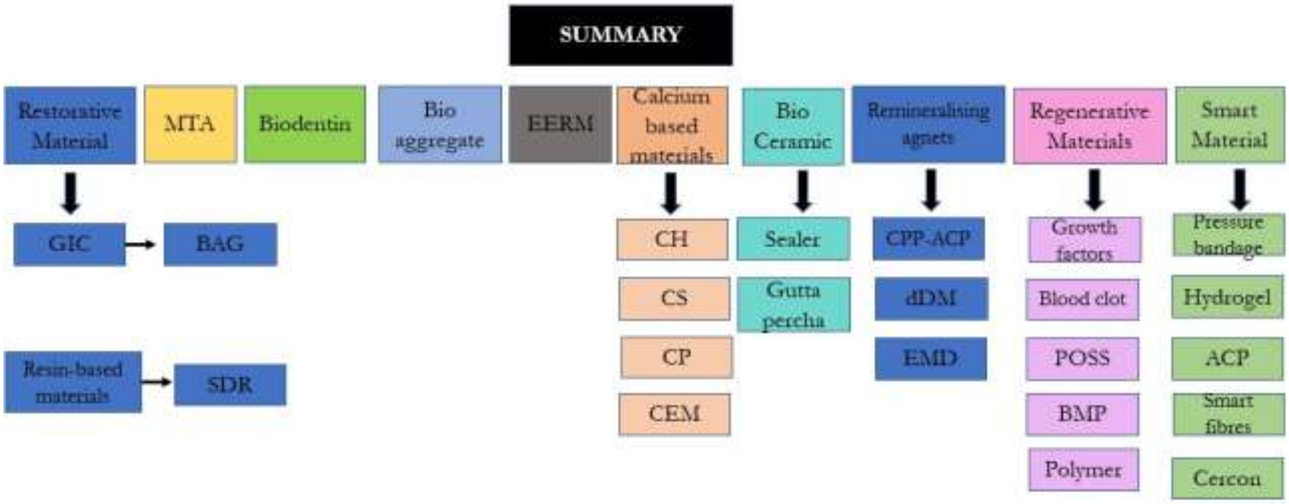


Fig 35:- Summary of Biomimetic materials.

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