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Review Article

BIOACTIVE ENDODONTIC MATERIALS-A REVIEW

Karthiga Senthil[2], Dr. Jayalakshmi[3], Dr.PadmaAriga*[1]
Professor, Department of Prosthodontics, Saveetha Dental College, Saveetha University
No.162 Poonamallae High Road, Velappanchavadi, Chennai 600077, Tamil Nadu.
Undergraduate, Saveetha dental college,
Saveetha Institute of Medical and Technical Sciences – SIMATS,
No.162 Ponamallae High Road, Vellapanchavadi, Chennai – 600077, Tamil Nadu.
Professor, Department of Conservative Dentistry and Endodontics
Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences - SIMATS
No.162 Ponamallae High Road, Velappanchavadi, Chennai- 600077, Tamil Nadu.
Email: padmanest@gmail.com

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Abstract

With an era of biomimetic dentistry, Bioactive materials prove useful as they promote biological healing and proves to be beneficial for the tissues.

Endodontic filling materials may be considered true implants as they touch and are meet the vital tissue of the tooth. They range from relatively specialised, highly biocompatible materials to new compositions for expanded use in restorative dentistry.

Bioactive materials and molecules having significant therapeutic benefits in

Some of endodontic therapy like Pulp-capping, Root Canal Therapy (RCT). This review paper highlights the properties, natural sources and clinical application of bioactive material and molecules in Endodontics.

Keywords: Bio active, Endodontics, Materials, Osteoinductive, Osteoconductive.

Introduction

Bioactive materials can be best defined as a compound when implanted into the body does not produce any injurious effects and also has the ability of eliciting a response from living tissue, organisms or cell such as inducing the formation of hydroxyapatite.

For a material to be Bioactive it must be bactericidal, bacteriostatic, sterile, stimulate reparative dentine formation, and maintain pulp vitality. A bioactive material consists of bioactive calcium phosphate ceramics, bioactive glass ceramics and bioactive composite[1].It can be used for dentinal tubule occlusion, regeneration of bone tissue, tooth remineralization, pulp capping material, permanent restorations and as asealer[2].

The aim of this article is to shed light on the properties of some of bioactive materials that is currently available.

Classification of Bioactive material:-

There are different types of bioactive materials like:-

(1) Class A Osteoinductive - They help the osteogenic precursor cell todifferentiate into bone matrix. Class A bioactivity occurs when a material elicits both an intracellular and an extracellular response at its interface.

(2) Class B Osteoconductive - They are capable sustaining cell attachment and consequent bone matrix apposition and formation. The material only has an extracellular response [3].

Calcium based materials

1) Calcium Hydroxide

Calcium hydroxide is a white odourless powder with the chemical formula $Ca(OH)2$ and a molecular weight of 7.08. Chemically, it is classified as a strong base in contact with aqueous fluids (its pH is about 12.5 - 12.8), and dissociate into calcium and hydroxyl ions. Calcium hydroxide is used and supplied in various forms[2]. It is used like a varnish when supplied as a liquid containing calcium hydroxide suspended in a solvent or when supplied as a paste in which calcium hydroxide is suspended in methylcellulose. Another form of calcium hydroxide is marketed as a base and a catalyst. By using the catalyst, calcium hydroxide reacts faster and forms a hard, amorphous compound within matter of minute in the oral environment. Finally, calcium hydroxide supplied as a paste contains a polymer resin that can be hardened when exposed to illumination from a handheld blue light source[3].

The release of hydroxyl ions in an aqueous environment is essential for the activation of calcium hydroxide against microbes. These ions reacted intensively with several biomolecules due to their highly oxidant free radicals[4]. As this reactivity is unspecified, the free radicals most likely gathered at the sites of generation. Hydroxyl ions have fatal effects on bacterial cells. They may damage the cytoplasmic membrane of bacteria, denature their proteins, or damage the DNA. It is difficult to prove which of these three mechanisms is mainly involved in the death of bacterial cells after their exposure to a strong base. Since enzymatic sites are located in the cytoplasmic membrane of bacteria, hydroxyl ions from calcium hydroxide exert their mechanism of action there. Extracellular enzymes favor digestion, and through hydrolysis act on nutrients, carbohydrates, proteins, and lipids, whereas intracellular enzymes act on the respiratory activity of the cellular wall structure[5].

The high concentration of hydroxyl ions from calcium hydroxide alters the pH gradient of the cytoplasmic membrane damaging its protein. The integrity of the cytoplasmic membrane is altered by the high alkalinity of calcium hydroxide by acting on the organic components and transporting the nutrients or by a saponification reaction in which the phospholipids or unsaturated fatty acids of the cytoplasmic membrane are destructed during the peroxidation process[6].

It is a material which works by its ionic effect. Chemical dissociation of calcium hydroxide occurs to form calcium and hydroxide ions which in turn act on the bacteria and tissues. The calcium acts by decreasing permeability of the capillary wall and decreasing the serum flow and inhibitory pyrophosphate activity[7]. The anti microbial activity is brought about by an elevated pH. The biological effects include secondary dentin formation over injured pulp. When used as a liner, it neutralises the acids which migrate towards the pulp and induces secondary dentin formation. When used a as a base it acts as a barrier against the penetration of irritating constituents from the restorative material and protects the dentinal tubules.

The standard material for pulp capping of normal vital pulp tissue is calcium hydroxide which have an anti-bacterial effect because of its high pH. Calcium hydroxide can induce profilaration, healing and repair of fibroblasts and therefore soft or hard tissue replacement can occur[8].

When the perforation is not treated immediately or in cases of wide perforation, in which profuse bleeding hampers the visualization, a calcium hydroxide [Ca(OH)2] dressing can be used previously. This procedure will prevent the growth of granulation tissue into the pulp chamber and will reduce the bacterial contamination into the underlying tissues[9]. The use of Ca(OH)2 is also indicated when there is not available time to perform the final treatment with MTA. When used as root canal dressing, complete removal of Ca(OH)2 from canal walls is not possible, regardless of the technique used. It is known that these residues adhered to the root canal walls negatively affect the prognosis of endodontic treatment, affecting the adhesion of the filling material to the canal walls and the cement penetration into dentinal tubules. Nevertheless, it has been shown that calcium hydroxide seriously impeded the healing process. Calcium hydroxide forms microscopic dentinal bridge that does not provide a continuous seal and bacterial leakage may happen, and its antimicrobial properties are lost[10] .

The success of calcium hydroxide as an endodontic medication is related to its ionic effect, produced by the chemical dissociation of hydroxide and calcium ions that act on the tissue and bacteria. These ions are responsible for the antimicrobial and biological properties of the medication, but calcium hydroxide is not equally effective against all microorganisms found in the root canal system. It has been reported that *Enterococus faecalis* shows resistance to high pH, ability to penetrate dentinal tubules and adaptation to different environmental conditions[11]. Moreover, a buffering effect of calcium hydroxide alkalinity by the dentin has been demonstrated and long-term calcium hydroxide as a root canal dressing may increase the risk of root fracture. Therefore, more effective alternatives to calcium hydroxide are still required.

2) Mineral Trioxide Aggregate(MTA)

Introduced in 1993 by Torabinejad, MTA is primarily made up of tricalcium silicate, dicalcium silicate and radiopaque filler and some traces of tricalcium aluminate and calcium aluminoferrite. The radiopacity is due to Bismuth oxide, Zirconia, or tantalum oxide[12].

Materials used to repair perforations should be well tolerated by peri-radicular tissues and should also provide a proper seal between the periapical tissues and the oral fluids. They should also be easy to handle, dimensionally stable, and radiopaque[13].

Mineral trioxide aggregate (MTA) is the most widely used material to seal perforations because induces regeneration of peri-radicular area, promotes a proper seal between the root canal, and the external surface of the root, sets in the presence of blood, and its biocompatibility. Past studies demonstrated that the sealing of furcation perforation with MTA presented great results with the rate of radiographic success higher than 82%[14].

However, MTA main disadvantages are the long setting time and the difficulty in handling.

MTA has been used in the apexification of immature roots as it facilitates development of normal periradicular structure by inducing formation of hard tissue barriers and formation of cementum surrounding MTA has been observed even after extrusion of MTA into a furcation.The other advantages include resistance to future bacterial penetration, has antibacterial activity on facultative bacteria, compatibility with the pulp and periradicular tissues, induces dentinogenesis, and has more dentinal bridging[15].

The mechanismof dentin bridge formation, when MTA is used as a direct pulp capping agent is that it induces cytologic and functional changes in the pulpal cells, resulting in formation of fibrodentine and reparative dentin at the surface of mechanically exposed dental pulp. Then it causes proliferation, migration and differentiation of odontoblast-like cells that produce a collagen matrix. This formed unmineralised matrix is then mineralised by osteodentin initially and then by tertiary dentin formation[16].

Silver Nanoparticles(AgNP's) with Mineral trioxide aggregate(MTA) showedhigher antibacterial and antimicrobial activity against Enterococcus faecalis, Candida albicans, compared to unmodified MTA.[17]

In a study carried out by Shabahang et al (1997),apexification in immature dog-teeth using MTA.It was proved that MTA induced hard tissue formation, resulting in root-end closure in 12 weeks[18].

3) Biodentine

Biodentine is a calcium silicate based material which consists of a powder and liquid component. The powder consists of tricalcium silicate, dicalcium silicate, iron oxide shade, and , calcium carbonate and oxide filler zirconium oxide. Tricalcium silicate and dicalcium silicate are used as main and second core materials, respectively, whereas zirconium oxide serves as a radiopacifier. The liquid, contains calcium chloride as an accelerator and a hydrosoluble polymer that serves as a water reducing agent[19].

Biodentine was specifically designed as a "dentine replacement" material. Biodentine has a wide range of applications including endodontic repair (root perforations, apexification, resorptive lesions, and retrograde filling material in endodontic surgery), pulp capping, and can be used under resin composite restorations. It presents good sealing ability, high compressive strengths, short setting time biocompatibility, bioactivity, and biomineralization properties.

It has antibacterial activity due to alkaline pH. This also helps in disinfection of the surrounding hard and soft structures of the tooth. It promotes pulp healing. It preserves the pulp vitality.Results of studies have shown that BAG can repair bone lesions through osteoblastic potential so it is logical that odontoblastic activity of BAG is survived[19].

It has the advantages of Reduced setting time, Better handling & manipulation, Improved mechanical property, Bioactivity when compared to MTA. It is used in a permanent restoration as a dentin substitute under the restoration, It can be used as a direct and indirect pulp capping material, in cases of partial pulpotomy and pulpotomy in primary molars, Apexication procedure, repair of perforated root canals and/or pulp chamber and as a root end filling material. Biodentine speeds up the formation of dentine barrier after direct pulp capping. In the first month, the quality of the dentine bridge formed with Biodentine is of better quality than that formed with calcium hydroxide[20]. The performance of Biodentine is equivalent to MTA.According to a study conducted by Machtou P, 2009 Biodentine does not require a two step obturation as in the case of MTA. As the setting is faster, there is a lower risk of bacterial contamination than with MTA.[21]

Bioactive glass is a material that is able to mineralize dentin, has antimicrobial effects in closed systems and may be used as endodontic medication . Unlike the calcium hydroxide, it has been reported that the antibacterial efficacy of bioactive glass increases when it is mixed with dentin[22]. In addition, these glasses release calcium, phosphate, sodium, silica and depending on liquid exchange in the environment, slowly transform into calcium phosphate. The bioactive glass suspension has shown to affect the mechanical properties of human root dentin in a lesser extent than calcium hydroxide .An ideal preparation of bioactive glass suspensions for root canal disinfection should combine the induction of high pH with the capacity for continuing release of alkaline species[23].

4) Root Repair Material (iRoot)

It is a calcium silicate material which is used for permanent root canal repair and filling applications. It is available in an injectable paste form and a putty form[24].It is made up ofcalcium phosphate,calcium silicates,zirconium oxide,calcium hydroxide.

The iRoot materials including iRoot SP, iRoot BP, and iRoot BP Plus, are calcium silicate-based bioceramic materials used as non-shrinking, insoluble, aluminum-free, and favorable biocompatible dentin substitutes. iRoot Fast Set root repair material (iRoot FS) is a modification of iRoot Putty Plus[25]. This modified material is biocompatible, non-mutagenic, non-allergic and well tolerated by subcutaneous tissue. Recent studies have demonstrated that iRoot FS has a faster setting time (within an hour) and hydrating process than MTA. iRoot SP exhibited significantly lower cytotoxicity and a higher level of cell attachment than MTA. iRoot FS also has a similar apical sealing ability as MTA [26]. iRoot SP has also shown in vitro to increase resistance to the fracture of endodontically treated roots, particularly when accompanied with bioceramic impregnated and coated gutta-percha cones. Fracture resistance was increased in simulated immature roots in teeth with iRoot SP[27].

5) Calcium Enriched Mixture Cement(CEM)

Asgary al. in 2006 introduced a novel endodontic material called CEM cement in dentistry because of its application in various endodontic procedures. CEM cement is believed to be similar to mineral trioxide aggregate (MTA), but with better physical properties. CEM cement is composed of different calcium compounds i.e. Calcium phosphate, Calcium hydroxide, Calcium sulfate, Calcium silicate, Calcium chloride, Calcium carbonate and Calcium oxide[28].

CEM cement is a white powder consisting of hydrophilic particles that sets in the presence of water base solution. Hydration reaction of powder creates a colloidal gel which then solidifies. It has the ability to form hydroxyapatite and hence biocompatible and forms an excellent physical and biological seal. It is an anti microbial and an anti fungal agent. It has the advantages of better flow, shorter setting time and less film thickness[29]. It has been used in Direct Pulp Capping, Pulpotomy, Root-end filling, Furcation Perforation, Resorption and Regenerative Endodontic treatment.

6) Calcium Phosphate

It is one of the oldest Bioactive materials. Amorphous Calcium Phosphate (ACP) is a mineral phase formed in mineralised tissues. It has the advantages of excellent bioactivity, high cell adhesion, adjustable biodegradation rate and good osteoconduction[30]. Calcium Phosphate Cement(CPC) is mixture of two calcium phosphate compounds, one acidic and the other basic. It is composed of tetracalcium phosphate and dicalcium phosphate reactants.CPC sets into hydroxyapatite. It has the ability to induce new bone formation.

It does not cause a sustained inflammatory response or toxic reaction. CPC implants are resorbed slowly and are replaced by natural bone in an approximate 1:1 ratio in an osteoconductive manner[31]. In the dentifrice, ACP along with fluoride, enhances remineralization and forms a strong bond to the dentin, becoming an intrinsic part of the tooth. Sealants containing ACP promote remineralization of carious lesions enamel surfaces[32].

7) Bioaggregate

It is an insoluble, radiopaque, and aluminium-free material primarily composed of calcium silicate, calcium hydroxide, and calcium phosphate. BioAggregate has been used to seal root-end filling. BioAggregate has the potential to induce odontoblastic differentiation and mineralization compared to that of MTA. It has the ability to promote the adhesion, migration, and attachment of human dental pulp cells, indicating its excellent cytocompatibility.It is non-toxic to osteoblast cells. It also enhances the expression of genes for collagen type 1, osteopontin and osteocalcin, which are genes associated with mineralization in osteoblast cells[33].

BioAggregate root canal repair filling material has been successfully developed as new generation of a dental root canal filling material by Innovative BioCeramix Inc. (IBC), which is a fine white hydraulic powder cement mixture for dental applications[34]. It utilizes the advanced science of nano-technology to produce ceramic particles that, upon reaction with water produce biocompatible and aluminum-free ceramic biomaterials. Upon mixing, the hydrophilic BioAggregate Powder promotes cementogenesis and forms a hermetic seal inside the root canal. It is effective in clinically blocking the bacterial infection, its ease of manipulation and superior quality makes BioAggregate the most innovative and unique root canal repair material. It is indicated in: repair of root perforation, repair of root resorption, root end filling, apexification, and pulp capping [35].

8) Endosequence root repair material

Endosequence Root Repair Material (ERRM) is a new bioceramic material consisting of calcium silicate, monobasic calcium phosphate, and zirconium oxide. The material has nanosphere particles with a maximum diameter of 1 x 10-3 μm that allow for the material to enter dentinal tubules, be moistened by dentine liquid, and create a mechanical bond upon setting[36]. They result in a gap-free interface between gutta-percha (GP), sealer and dentin. It is antibacterial because of their highly alkaline Ph and has great biocompatibility,and promotes osteogenesis and biomineralisation[37]. EndoSequence root repair material putty and EndoSequence root repair material paste have been developed as ready-to-use, premixed bioceramic materials recommended for perforation repair, apical surgery, apical plug, and pulp capping. The manufacturer stated that the moisture present in the dentinal tubules is adequate to allow the material to set. EndoSequence is stated by the manufacturer to bond to adjacent dentine, to have no shrinkage, and to be highly biocompatible, hydrophilic, radiopaque, and antibacterial due to a high pH during setting. The major advantages of this material are improved handling characteristics over traditional MTA and the delivery of a consistent product with each application[38].

This material is bioactive due to its ability to form a hydroxyapatite or apatite-like layer on its surface when it comes in contact with phosphate-containing fluids. Hansen et al. compared the diffusion of hydroxyl ions for ERRM and WMTA through root dentine. They found that although both materials showed diffusion of ions through dentine, the effect was less pronounced and of shorter duration for EndoSequence than WMTA[39].

9) MTYA1-Ca filler

Atsuko Niinuma(1999) developed resinous direct pulp capping agent containing calcium hydroxide. The powder consists of 89.0% microfiller, 10.0% calcium hydroxide and 1.0% benzoyl peroxide mixed with liquid. MTYA1-Ca developed dentine bridge formation without formation of a necrotic layer, revealed to have good physical properties[40].

10) Theracal

It is a light-cured, resin-modified calcium silicate filled base or liner for use in direct and indirect pulp capping and as a protective base or liner under composite, amalgam, cements. It can be used in place of calcium hydroxide, RMGI, IRM/ZOE, glass ionomer and other restorative materials. It consists of 45% weight Type III Portland cement 10% weight Radiopaque content 3. 5% weight hydrophilic thickening agent (fumed silica) and 4. 45% resin which consists of a hydrophobic component consisting of Urethane Dimethacrylate (UDMA), Bisphenol A-Glycidyl Methacrylate (BisGMA), Triethylene Glycol Dimethacrylate (TriEDMA or TEGDMA) and a hydrophilic component consisting of Hydroxyethyl methacrylate (HEMA) and Polyethylene glycol dimethacrylate (PEGDMA) Theracal acts as a barrier and protectant to the dental pulpal complex[41]. It has lesser solubility and high calcium release. Theracal allows us to complete Direct/Indirect pulp capping procedure very easily within the single appointment without any operator error. Its setting time is controllable hence there is no problem of solubility while setting. Also the chairside time is less as compared to other materials because there is no need to mix or manipulate Theracal as it is available in Syringe and disposable tips[42].

Calcium release promotes hydroxyapatite formation and therefore secondary dentin formation and acts as a protective seal for the pulp. It has an alkaline pH which promotes healing and apatite formation.

A study by Bisco inc. concluded that the Calcium release after 24 hours of Theracal was significantly more as compared to reference pulp capping material Dycal. Theracal LC had the greatest amounts of compressive and flexural strengths at all time periods[43].

Theracal released less Calcium ions as compared to MTA Plus gel and Biodentine but more than that by Dycal. Porosity, Water sorption and Solubility were last seen with Theracal as compared to other materials like Dycal, MTA Angelus, Biodentin , MTA plus etc. The thickness, continuity of Calcium Phosphate deposits after aging was last seen in TheraCal. (Gandolfi et al., 2015)[44].

Some of the important advantages of Theracal are A) Improved Physical and chemical properties because it had overcome the shortcomings of MTA due to light curing and ability to complete the treatment within single appointment. B) Excellent Handling characteristics leading to decreased operator error and Good Sealing property. C) Good antimicrobial and cytocompatibility property. D) Mild nature to the pulp due to alkaline pH.

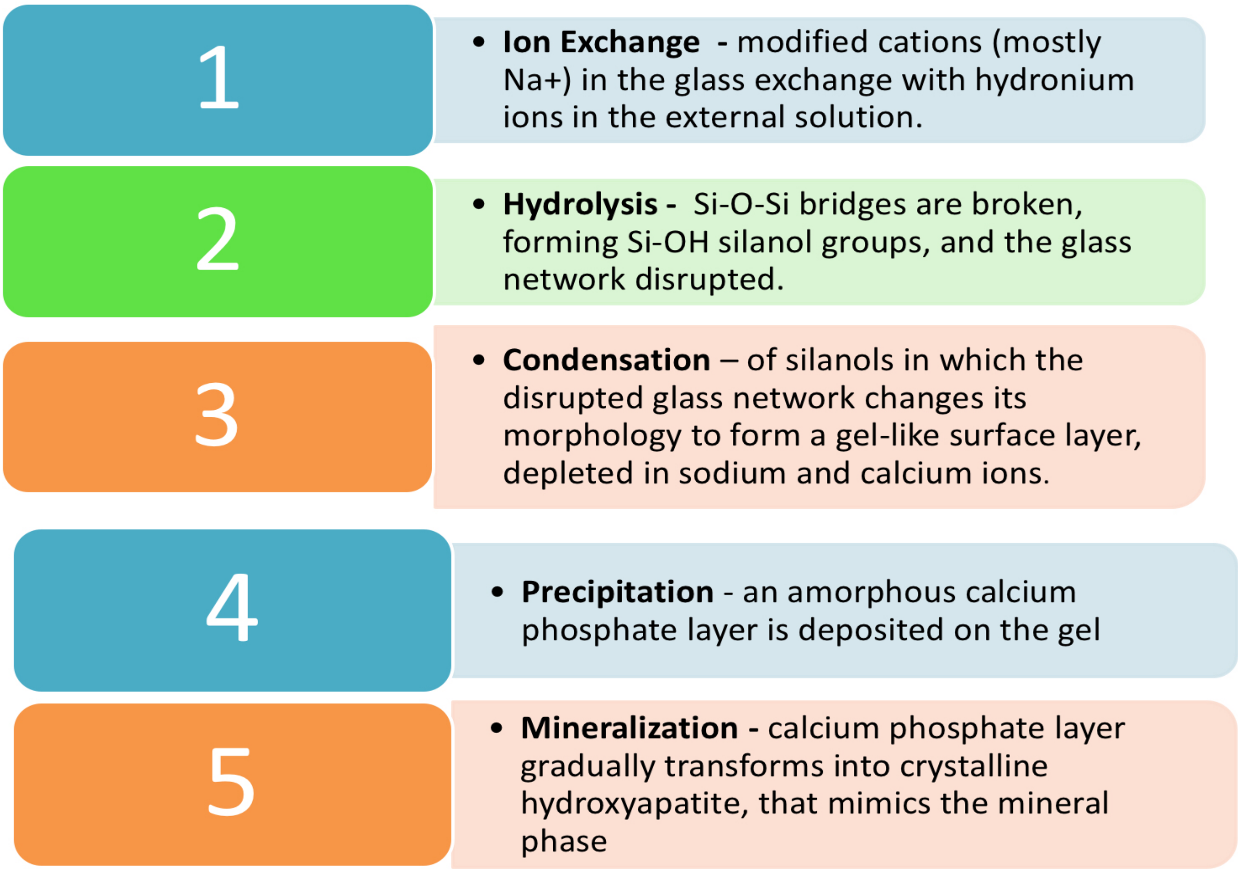
11) Bioactive Glass

Bioative glasses of the SiO2-Na2O-CaO-P2O5 system have been shown to possess antimicrobial activity through the release of ionic alkaline species.

These can be used as dentine disinfectants to offer an alternative to calcium hydroxide[20].

Those in the form of amorphous nanoparticles with a size of 20 to 60 nm may show an advantage over micron-sized material, because the decrease in glass particle size should increase, by more than 10-fold, the active exchange surface of glass and surrounding liquid.

In turn, this would substantially increase ionic release into suspension and enhance antimicrobial efficacy[45].



Others:-

1) Chitosan

Chitosan (poly (1, 4), b-d glucopyranosamine) is obtained from deacetylation of chitin.

Chitosan is an excellent bioadhesive that possesses broad spectrum of antimicrobial properties.

Antibacterial activity is due to the electrostatic attraction with the negatively charged bacterial cell wall, which leads to the altered cell wall permeability, resulting in leakage of the proteinaceous and other intracellular components followed by the death of the cell[46]. It has the ability to inhibit the formation of biofilm and has antibacterial effect.

Chitosan exhibits some properties, which make it attractive for usage in dental medicine in order to increase the wound healing process. Chitosan possesses antibacterial effects enhances the wound healing by establishing optimal environmental conditions is biocompatible and does not interfere with human immune system[47].

2) Castor bean oil

It consists of 81-96% triglyceride of ricinoleic acid, and is considered a natural polyol containing three hydroxyl radicals. COB or RCP (Ricinus Communis Polyurethane) was developed as a biomaterial for bone repair and regeneration of bone following a local bone damage. The material is considered to be an excellent candidate for use in pulp capping[48].

Conclusion

Materials used in Endodontics are placed in direct contact with vital periapical tissues. Hence, the tissue response to these materials becomes important and biocompatibility of the materials should be evaluated for successful outcome of the treatment. There is much room for the improvement and further development of materials used in dentistry. The most sophisticated class of Bioactive materials in the foreseeable future will be that which emulate biological systems.

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Corresponding Author:

Dr. PadmaAriga*,

Email: padmanest@gmail.com