Nano-hydroxyapatite and its contemporary applications

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Abstract

Combination of nano-sized hydroxyapatite (nHA) with restorative materials like glass ionomer cement and composite resins has been reported recently in 2011. The documented effects of these nano-sized particles on the chemistry of these materials include increased biocompatibility and mechanical strength. nHA has been utilized for various applications like pulp capping agent, root canal sealer, filler for bleaching agents and toothpastes, osseo-conductive bone graft etc., A nHA has been obtained using natural bovine bone, carbon template technique, hydroxyapatite-chitosan template technique, wet precipitation technique, plasma spraying technique etc. This paper presents a review of the various aspects of nHA and summarizes the methods of fabrications and potential clinical applications of the same.

Crystallography and chemical composition to that of human hard tissue.[7] On account of its outstanding properties like biocompatibility, bioactivity, osteoconductivity, non-toxicity and non-inflammatory nature,[6] this bioceramic has got a variety of applications which include: Bone tissue engineering; restoration of periodontal defects;[7,8] orthopedic and dental implant coating,[10‑12] endodontic treatment like pulp-capping, repair of mechanical bifurcation perforations and apical barrier formation,[13‑15] fillers for reinforcing restorative glass ionomer cement (GIC)[16‑22] and restorative composite resin;[23‑37] desensitizing agent post bleaching;[38] for treating early carious lesions[39‑41] and as a remineralizing agent in toothpastes.[42]

In an article in 1975, Nery et al., for the first time in dentistry, studied the effect of tricalcium phosphate reagent in intrabony defects in dogs, but later it was demonstrated that the phosphate was a mixture of hydroxyapatite and tricalcium phosphate.[43,44]

Hydroxyapatite is manufactured in many forms and can be prepared as a dense ceramic,[45] powder,[46] ceramic coating[47] or porous ceramic[48] as required for the particular applications. However, in recent years, nano-sized hydroxyapatite (nHA) with appropriate stoichiometry, morphology and purity have

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stimulated great interest in scientific research. It is believed that nHA with grain size <100 nm in at least one direction has a high surface activity and ultrafine structure similar to the mineral found in hard tissues [Figure 1].[49]

With the advent in technology and developing interest, diverse methods for fabricating hydroxyapatite have been reported in the literature. According to a review published by Sadat-Shojai et al., various methods for preparing hydroxyapatite can be widely classified into dry methods, wet methods, high temperature processes, synthesis from biogenic sources and combination of above-stated procedures [Table 2].[49]

Among all the methods, chemical precipitation, combination methods and hydrothermal processes are the most popular methods for fabricating nHA.

The mechanical properties of hydroxyapatite are greatly determined by the morphology and crystallography of the particles, which in turn demands on the mode of fabricating Hydroxyapatite.

Materials and Methods

The electronic database chosen for developing this review was PubMed database. Following keywords were used for searching relevant papers: (nanohydroxyapatite or hydroxyapatite) and (dental restorations or restorative material or composite resins or GIC or pulp capping agents or root canal filling agents). Papers were selected if the combination of words appeared anywhere in the paper, were published over the time period of 25 years (1987-2012) and were written in English. The reference list of each paper was reviewed and any paper appearing in the reference list was added to the list of papers to be manually reviewed. A total of 127 papers were retrieved from the PubMed database, out of which only 39 papers were chosen which presented the use of hydroxyapatite particularly in restorative dentistry. The remaining papers listed in the reference list of this paper are regarding the various techniques of manufacturing hydroxyapatite and the conventional restorative materials used in dentistry.

The main aim of this paper is to review the literature for various studies done on hydroxyapatite as a restorative material for various clinical use.

Results of Restorative Applications of nHA

Fillers in restorative GICs

The first glass ionomer material was introduced by Wilson and Kent in 1972 as a “new translucent dental filling material” recommended for the restoration of cervical lesions.[9,31] The glass ionomer family of restorative materials has evolved over the past 40 years into a diverse group of products including liners, bases, restorative materials, luting agents as well as pit and fissure sealants; all available in both the conventional and resin modified varieties.[31] The vast indication of GIC is attributed to their beneficial properties, which include fluoride release and recharge ability, marginal sealing, chemical bonding to dental structure, biocompatibility and coefficient of thermal expansion similar to that of the tooth structure. Despite these outstanding advantages, there are well-known shortcomings associated with GIC, such as the sensitivity to moisture contamination and desiccation and poor mechanical properties.[22]

The effect of adding hydroxyapatite to GIC was first studied by Nicholson et al.[16] in 1993 and since then has directed research in this field.

A study by Yap et al.[17] stated that addition of hydroxyapatite particles of the size range from 0.3 to 50 microns 12% by volume to restorative GIC would result in improvement of mechanical properties.

![Figure 1: Field emission-scanning electron microscopy image of nanosized hydroxyapatite](image)
Arita et al.\cite{18,19} in their study have reported that adding nHA (Whiskers and Granules) improved the flexural strength and microstructural properties of GIC. While whiskers showed better strength, granules when added 8% by mass also improved the flexural strength. The same author carried out another study in 2011\cite{22} in which hydroxyapatite particles of varying sizes were added to GIC 8% by mass to enhance the mechanical and chemical properties of the cement. They concluded that conventional restorative GIC can be improved by incorporating highly reactive hydroxyapatite particles of 10 microns diameter.

Gu et al.\cite{20} carried out the addition of zirconia powder with nHA in restorative GIC and achieved improved mechanical properties over hydroxyapatite when used alone. Such difference in the results was attributed to high strength, high modulus, hardness and insoluble nature of zirconia.

In a study conducted by Lee et al.\cite{21} the bond strength and resistance to demineralization was significantly enhanced by adding 10% nanoscopic hydroxyapatite.

Goenka et al.\cite{24} formulated bioactive nanocrystalline calcium deficient hydroxyapatite (nCDHA) GIC composite cement by adding nCDHA (5, 10 and 15 wt %) to conventional glass powder. They concluded that the addition resulted in increased compressive strength and resorption potential of the cement.

**Fillers in restorative composite resin**

Composite resins have been introduced into the field of conservative dentistry to minimize the drawbacks of the acrylic resins that replaced silicate cements (the only aesthetic materials previously available) in the 1940s. In 1955, Buonocore\cite{25} used orthophosphoric acid to improve the adhesion of acrylic resins to the surface of the enamel. In the year 1962 Bowen\cite{26} developed the Bis-phenol A-glycidyl methacrylate (Bis-GMA) monomer in an attempt to improve the physical properties of acrylic resins, as their monomers only allowed linear chain polymers to be formed. Today most composites used in dentistry are hybrid materials, so-called because they are composed of polymer groups reinforced by an inorganic phase of glass fillers with different compositions, particle sizes and fill percentages. Flowable or condensable composites have attempted to provide an answer to certain functional requirements, although they have not been too successful at improving properties. Turning to polymerization initiators, both conventional or high intensity halogen lamps and light-emitting diode curing lights which provide a gradual increase in light intensity are very useful for reducing shrinkage of the composite material.\cite{27} The clinical choice of a composite must consider whether priority should be given to mechanical or esthetic requirements: If mechanical considerations are paramount the material with the greatest volume of filler will be chosen; if aesthetic considerations predominate, particle size will be the most important factor. Additional components such as opaquers and tints make it possible to improve the aesthetic results.\cite{28} Despite the significant improvement of resin-based composite, restorative composites still suffer from two key shortcomings: Deficiencies of mechanical strength and high polymerization shrinkage, which are responsible for the shorter median survival lifespan of resin based composites (5-7 years) in comparison with amalgam (13 years).\cite{29,30,31}

Addition of hydroxyapatite as a filler particle to composite resin was first reported in 1988 by Okazaki and Ohmae\cite{32} which resulted in improvement of mechanical properties and biocompatibility only when the apatite to resin ratio was maintained at 1.

Dupraz et al.\cite{33} investigated the effect of different coupling agents on the hydroxyapatite powder incorporated into composites as filler.

Santos et al.\cite{34} incorporated hydroxyapatite fillers (silane treated and untreated) into the Bis-GMA polymer. The effect of silane treating hydroxyapatite particles resulted in better contact with the polymer matrix. A similar study was carried out by the same authors in 2002\cite{35} for studying the water absorption characteristics. They reported that lower water uptake was seen when silane treated hydroxyapatite were incorporated in composite, but the water solubility increased with more incorporation of hydroxyapatite.

Arcis et al.\cite{36} proposed that addition of hydroxyapatite should be 50-60 wt % to enhance the mechanical properties. The author preferred microscopic hydroxyapatite over nHA as filler particles.

Domingo et al.\cite{37} also suggested that nanometric particles as filler were unsuitable for clinical purpose. According to the author, micrometric filler particles exhibited better hydrolytic stability.

In contrast to the past, a recent report of Sadat-Shojai et al.\cite{38} described a significant increase in bulk mechanical properties and bond strength to dentine on adding hydroxyapatite nanorods (0.2-0.5 wt %).

According to a study performed by Chen et al.\cite{39} the critical mass fraction of nHA fibers in resin should be around 10% to influence the strength and mechanical properties.

Zhang and Darvell\cite{40} demonstrated a positive variation in mechanical properties with the addition of hydroxyapatite whiskers. This variation was conferred due to properties like good dispersibility and wettability of the whiskers with the polymer. In the same year, Zhang and Wang\cite{41,42} showed accelerated photopolymerization of self-etching adhesive incorporated with hydroxyapatite.
Pulpotomy and direct pulp capping agent
The osseointegrative property of hydroxyapatite was exploited for the purpose of pulp capping and pulpotomy back in 1992 by Jaber et al.[54] In his animal study, hydroxyapatite was compared with calcium hydroxide as a pulp capping agent which showed a negative result as hydroxyapatite caused dystrophic calcification in pulp, hence interfering with the future endodontic treatment.

In a similar study by Sübay and Aşci,[55] hydroxyapatite as a direct pulp capping agent did not induce hard tissue bridging at the pulp exposure site.

Hayashi et al.[56] conducted an animal study and concluded that hydroxyapatite could directly substitute osteodentin when used as direct pulp capping agent.

In an article in 2010, Shayegan et al.[57] have reported that nHA did not cause any pulp inflammatory response when used as direct pulp capping agent while Shinkai et al.[58] reported no significant changes on mixing hydroxyapatite in adhesive systems for dentine bonding or direct pulp capping.

Kato et al.[59] in an animal study evaluated the histopathological and immunohistochemical changes in pulp on adding different forms of calcium phosphate to adhesive resin for the purpose of direct pulp capping. The results showed that hydroxyapatite and beta tricalcium phosphate had a tendency to produce a larger amount of reparative dentine.

Fillers in endodontic root canal sealers
Hydroxyapatite was added to endodontic sealers by Gambarini and Tagger[60] in 1996 as it was thought to influence the apical healing and sealing ability. He concluded that it did not adversely affect the sealing properties. In a recent report by Collares et al.[61] adding nHA up to 40% to root canal sealers did not alter its radio opacity and film thickness.

Treatment of early carious lesions
Li et al.[62] in 2008 referred as the “natural building blocks” of enamel. According to them 20 nm sized hydroxyapatite particle can effectively remineralize the enamel.

In the year 2011, Huang et al.[63] proved with the help of an in vitro study that nHA can be used as an effective repair material and antacaries agent with pH < 7. He also reported that adding Galla chinesis along with nHA had a synergistic effect on the remineralization of carious enamel.[64]

Conclusion
It may be stated that nHA is a versatile material with a multitude of applications in various dental materials. Although proven to have a significant impact on the properties of the material it reinforces, more studies are required, especially to test and quantify its efficacy under clinical conditions.

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Kantharia, et al.: Restorative applications of nano-hydroxyapatite


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