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APPLICATION OF NANOBIOMATERIALS IN RESTORATIVE DENTISTRY

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ABSTRACT
Nanodentistry is defined as the science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured material. Varieties of new dental products are available that rely on nanoscale properties, ranging from implants to oral hygiene products. Nanodentistry encourages the concept of minimally invasive dentistry, creating a more dentist friendly atmosphere. However, patient awareness and education is important to make them understand the developments in the field and the options available in the treatment. Following the progress of nanotechnology, current dental research is exploring designs for restorative systems. During the last decades, an increasing variety of dental restorative materials were developed. The paper reviews the most innovative nanocomposites, their structure, antibacterial and remineralizing capabilities, economical and ethical aspects and safety issues.

Key words: nanodentistry, dental restorative materials, nanocomposites

INTRODUCTION
Nanotechnology was first described in 1959 by Richard P Feynman, and has since been a part of scientific theory with potential medical and dental applications since the early 1990s.

Nanotechnology, also commonly referred to as molecular nanotechnology or molecular engineering, is the production of functional materials and structures that are in the range of 0.1 to 100 nanometres (the nano scale) by various physical or chemical methods. The intense interest in using nanomaterials stems from the idea that they may be used to manipulate the structure of materials to provide dramatic improvements in electrical, chemical, mechanical and optical properties [1]. In theory nanotechnology can be used to make products lighter, stronger, cheaper and more precise. Working at natures scale the nanoscale, researchers are making exciting advances in applying nanotechnology to meet challenges in medicine and dentistry.

Nanodentistry is defined as the science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured material. Varieties of new dental products are available that rely on nanoscale properties, ranging from implants to oral hygiene products. Nanodentistry encourages the concept of minimally invasive dentistry, creating a more dentist friendly atmosphere. However, patient awareness and education is important to make them understand the developments in the field and the options available in the treatment [2].

Following the progress of nanotechnology, current dental research is exploring designs for restorative systems. In the last 10 years numerous theoretical predictions have been made based on the potential applications for nanotechnology in dentistry, with varying levels of optimism [3].

During the last decades, an increasing variety of dental restorative materials were developed. Great strides in dental research have led to a variety of alternatives to amalgam [1]. Gold and ceramics are the main standard material used for indirect restorations, and until the late seventies amalgam was used for direct restorations [4]. The use of amalgam has been critically discussed due to its allergic and toxic potential upon mercury release [5]. Great strides in dental research have led to a variety of alternatives to amalgam [6]. An increased demand for direct filling materials was supported by changes in restorative techniques. The development of restorative materials presents the modern dentist with several choices when selecting the best restorative material to restore cervical cavities on teeth. Amalgam, composite resin (in different formulations), glass ionomer, resin modified glass ionomer and compomer may all be considered appropriate restorative materials for Class V restorations [7]. The most common, next to amalgam, are resin composites. Resin composites are the most esthetically accepted material with satisfactory physical properties [8]. They were introduced into the field of conservative dentistry to minimise the drawbacks of the acrylic resins that had replaced the silicate cements in the 1940s.

Structure

Dental composites are basically composed of three chemically different materials: the organic, polymeric matrix formed by polymerization of one or more monomer/oligomers (organic phase); the inorganic matrix (filler of various types - silica, ceramic etc., sizes, shapes and morphologies, or disperse phase); and an organosilane - a coupling agent to bond the filler to the organic resin (interfacial or interphasial phase).

Usually the organic matrix is based on methacrylate chemistry, especially cross-linking dimethacrylates like: 2,2-bis[4,2-hydroxy-3-methacryloyloxypropyl)phenyl]propane (Bis-GMA), ethoxylated Bis-GMA (Bis-EMA), 1,6-bis[2 methacryloyloxyethoxy-carbonylamino]-2,4,4-trimetylhexane (UDMA), triethylene glycol dimethacrylate (TEGDMA) – Fig. 1. [9-11].

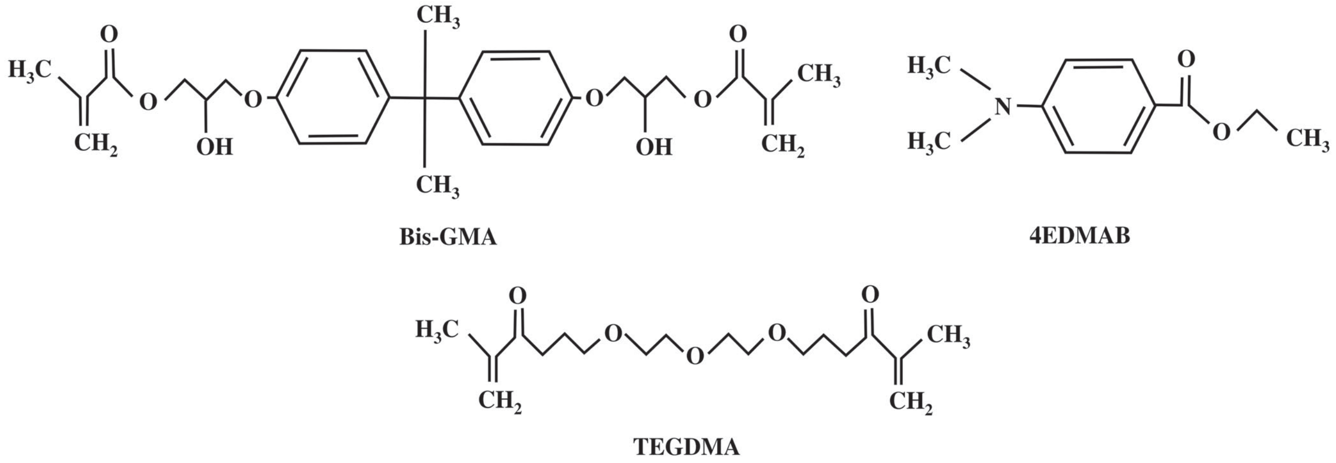

Fig 1. The molecular formula of common dental monomers and initiator.

The free radical polymerization of the matrix monomers leads to a three-dimensional network. Most of the contemporary dental polymer composites are light curing composites which polymerize, harden by irradiation with visible light in the wavelength range 400-500 nm. Nearly all composite manufacturers are using camphorquinone as the photoinitiator, with absorption maximum at 468 nm.

The Bis-GMA monomer was developed in 1962 in an attempt to improve the physical properties of acrylic resins, since their monomers only allowed linear chain polymers to be formed. These early composites, which were chemically cured, required that the base paste be mixed with the catalyst, leading to problems with proportions, with the mixing process and color stability. During the initial development of dental composites it was shown that the acquisition of good properties in the composite was dependent upon the formation of a strong bond between the inorganic filler particles and the organic polymer matrix.

When inorganic phases in an organic/inorganic composite become nano-sized, they are called nanocomposites. The interest in using such nanomaterials originates from the idea that they can provide dramatic improvements in electrical, optical, chemical and mechanical properties.

Nanofillers are very different from traditional fillers. The types of nanofillers in dental composites included silica [12, 13], tantalum ethoxide [14], zirconia-silica [15], alumina [16], nano-fibrillar silicate [17], ordered colloidal particles [18], and titanium oxide [19]. Nanoparticles were used either as the sole filler of the composite [12], or in combination with other types of fillers [20, 21]. To prepare nanofillers various techniques are used like flame pyrolysis, flame spray pyrolysis, and sol-gel processes.

Nanohybrid and **nanofilled** resin based composites are generally the two types of composite restorative materials referred to under the term “nanocomposite”, usually in a context of particle size. ***Nanohybrid types*** contain milled glass fillers and discrete nanoparticles (40 – 50 nm) and ***nanofill types*** contain nano-sized filler particles, called *nanomers* (NM) and agglomerations of these particles described as *nanoclusters* (NC). The nanomeric particles are monodisperse non-aggregated and non-agglomerated silica nanoparticles.

Development on resin based composites during the last decade has generated different subspecies of restorative materials like the hybrid resin composites, the fine hybrid resin composites, and the microfill composites.

The ***hybrid composites*** contain large filler particles of an average size of 15-20 μm and also a small amount of colloidal silica with particle size of 0.01-0.05 μm [22]. ***Microfilled composites*** contain amorphous silica. They were developed to address the polishing requirements of anterior restorations. These silicon dioxide particles are submicroscopic, averaging approximately 0.04 ìm in diameter, though the size varies among materials. Because the filler particles in a microfilled composite are so small, they have from 1,000 to 10,000 times as much surface area as filler particles in conventional composites. The increased surface area must be wetted by the monomer matrix, which results in a significant increase in viscosity. This increase in viscosity limits the percentage filler content of the composite to approximately 35 wt%, which in turn limits the strength and stiffness of the composite [23, 24].

While some studies demonstrated that hybrid and microfilled composites have similar performance in aesthetic cavities, others concluded that microfilled composites are the best option for anterior cavities because of their high translucency, high polish, and polish retention. Hybrid and microhybrid composites have traditionally been used for posterior restorations due to their high strength. However, no one composite material has been able to meet both the functional needs of a posterior Class I or Class II restoration and the superior aesthetics required for anterior restorations. This raised the need to develop novel nanofillers and then - the new category of resin composites - the nanocomposites, using advanced methacrylate resins and curing technologies [25].

There are two types of ***nanocluster*** fillers. The **first type** consists of zirconia-silica particles synthesized from a colloidal solution of a zirconyl salt and silica. The primary particle size of this NC filler ranges from 2-20 nm, while the spheroidal agglomerated particles have a broad sized distribution with an average particle size of 0.6 ìm. The **second type** of nanocluster filler, which was synthesized from 75 nm primary particles of silica, has a broad secondary particle size distribution with a 0.6 ìm average. These silica particles were treated with 3-methacryloxypropyltrimethoxysilane (MPTS), as a coupling agent that contains a silica ester functional group on one end for bonding to the inorganic surface, and a methacrylate group on the other to make the filler compatible with the resin before curing to prevent any aggregation or agglomeration [10, 15, 26].

Extremely small filler particles are with dimensions below the wavelength of visible light (0.4 - 0.8 ìm), and hence they are unable to scatter or absorb visible light. Thus, nanofillers are usually invisible and render the advantage of optical property improvement.

Due to their small particle sizes, nanofillers can increase the overall filler level. Since polymerization shrinkage is mainly because of the resin matrix, the increase in filler level results in a lower amount of resin in nanocomposites and will also significantly reduce polymerization shrinkage and dramatically improve its physical properties. Increasing the filler fraction is a good strategy for improved mechanical performance. A higher filler fraction helps in increasing the fracture toughness because fillers decrease the volume of the weak polymer matrix and act as toughening sources, besides increasing the elastic modulus. Filler packing is also influenced by the size, arrangement, distribution and shape of the particles.

Nanohybrid composites possess a wider range of particle sizes, and multiple filler compositions. A commercially available nanohybrid composite is composed of 3 different types of filler components: non-agglomerated discrete silica nanoparticles, prepolymerized fillers (PPF), and barium glass fillers. The non-agglomerated "discrete" silica nanoparticles are spheroidal and about 20 nm in size. The prepolymerized fillers are about 30-50 µm in size, while the barium glass filler comes with an average particle size of 0.4 µm. This combination of three fillers allows for increased filler loading of 84% by weight and 69% by volume. The discrete unassociated nanoparticles that are well-dispersed in the matrix on a nanoscale level allow for an increased filler loading and reduced viscosity of nanocomposite, thus resulting in increased hardness, abrasion resistance, fracture resistance, polishability, and in reduced polymerization shrinkage (1.4% to 1.6% by volume) and shrinkage stress. As the inter particle dimension decreases, the load-bearing stress on the resin gets reduced, thereby inhibiting crack formation and propagation. The spheroidal shape of the nanoparticles provides smooth and rounded edges, thereby distributing stress more uniformly throughout the composite resin.

Using statistically designed experimentation methodology many combinations of NC and NM fillers were studied to determine an optimal formulation for agglomerated cluster/fine-particle nanofill restorative dental nanocomposite (Filtek™ Supreme - 3M ESPE). The formulation for the dentine, body and enamel shades of Filtek Supreme Standard pastes contain zirconia-silica NCs and silica NPs. The effective primary particle size is 20 nm. The formulations of Filtek transluscent shades contain a filler predomentally composed of individual NM particles 75 nm in diameter and a minor amount of silica NCs. This would result in a smoother surface than would breakage of the much larger, nonsubdividable particles contained in many hybrids [15].

Ormocer® is a registered trademark of Fraunhofer-Gesellschaft (Munich, Germany), an acronym for **organically modified ceramics**. This is a new technology based on sol-gel synthesis using particles comprising silicones, organic polymers, and ceramic glasses that is applicable to dental composites. In contrast to conventional composites, the ormocer matrix is not only organic but also inorganic. Therefore monomers are better embedded in the matrix what reduces the release of monomers. Ormocer basically consist of three components – organic and inorganic portions and the polysiloxanes. The proportions of those components can affect the mechanical, thermal and optical qualities of the material:

1. The organic polymers influence the polarity, the ability to cross link, hardness and optical behaviour.
2. The glass and ceramic components (inorganic constituents) are responsible for thermal expansion and chemical stability.
3. The polysiloxanes influence the elasticity, interface properties and processing [27].

Ormocer® composite technology is used in conjunction with nanoparticle fillers such as ZrO_2 that are widely used in nanocomposite restorative systems. Some ormocers (such as CeramX™ - Dentsply International) contain particles as small as 2–3 nm in diameter.

Commercially available is ormocer-based, nano-ceramic nanocomposite. It contains glass fillers (1.1 - 1.5 µm), but differs from the conventional hybrid composites in two main features - a methacrylate-modified silicon-dioxide-containing nanofiller (10 nm) substitutes the microfiller typically used in hybrid composites (agglomerates of silicon dioxide particles); the conventional resin matrix is replaced by a matrix full of highly dispersed methacrylate-modified polysiloxane particles (2 - 3 nm). These nanoceramic particles are organic–inorganic hybrid particles. Both the nanoceramic particles and nanofillers have methacrylate groups available for polymerization [28].

Modifying ormocers with organic moieties such as methacrylate-substituted ZrO_2 or SiO_2 organosol nanoparticles was found by Moszner et al to improve the mechanical properties of resin-based composites [29]. This study also describes ormocers as being more biocompatible, confirmed by a manufacturer (Voco GmBh). Ormocers also claim decreased surface roughness, which is supported by *in vitro* evidence involving a variety of polishing techniques [30, 31].

Antibacterial and remineralizing capabilities of nanocomposites

The nanocomposites possess antibacterial and remineralizing capabilities. Such a combination of capabilities is highly beneficial to inhibit caries, but is unavailable in any current restorative materials. Nanocomposite-containing nanoparticles of amorphous calcium phosphate (NACP), nanoparticles of silver (NAg), and quaternary ammonium dimethacrylate (QADM) had strong antibacterial capabilities that were maintained in a 180-day water-aging experiment. Mechanical strength and elastic modulus of nanocomposite after 180-day water-immersion matched those of commercial control composites without antibacterial properties. Incorporation of QADM into NACP nanocomposite greatly reduced biofilm viability, metabolic activity, colony-forming unit counts (CFU), and lactic acid production. The antibacterial results were not significantly different after water-aging for 1, 30, 90, and 180 days. The durable antibacterial properties, plus the calcium (Ca) and phosphate (P) ion release and acid neutralization properties, indicate that the novel nanocomposite may be useful in restorations to inhibit secondary caries.

Silver has been used for its bactericidal properties for many years. The antimicrobial, antifungal and antiviral action of silver or silver compounds is proportional to the amount of released bioactive silver ions (Ag+) and its availability to interact with bacterial or fungal cell membranes [32]. Silver has been used in ionised and elementary forms, as silver zeolites or as nanoparticles [33]. The advantage of nanoparticles is the smaller-size that show stronger antibacterial activity due to their higher surface area to volume ratio [34].

Composite resins modified by microparticulated silver revealed antiadherence activity and bactericidal effect against *S. mutans* [35]. Orthodontic adhesives with nanosilver particles had their antibacterial capacity raised without compromising physical properties [36].

Economical and ethical aspects

Depending on its innovativeness, it is considered that the costs of introducing a new dental restorative materials could be estimated at several hundred millions. Although prices paid by patients over time will steadily drop, initially restorative dental nanomaterials will be costly since companies have to recover substantial investments. Personalized sanation plan in dental treatment may prove to be a financial burden as it stimulates the use of costly preventive approaches. On the positive, it is also claimed that nanotechnology will make certain processes faster and cheaper. Moreover, it is also argued that nanomedicine on the longer run will reduce societal and economic costs associated with healthcare and improve clinical outcomes for the patient at the same time. Like with other mass produced high tech products, scaling up the production of dental restorative nanomaterials will lower the prices rapidly.

Regarding special characteristics of the risks for dental nanomaterials, another related problem must be considered, namely informed consent. Although often brought up in relation to the clinical studies of dental nanomaterials it could also be framed as a general concern to applying of nanomaterials for medical purposes in general. The notion 'informed' encompasses disclosure and comprehension of the technology being used, including any known risks and benefits. 'Consent' includes voluntariness, competence and agreement of the person affected. This implies that affected persons voluntarily agree to subject themselves to the technology. As long as nanomaterials are associated with risks, but also with significant uncertainty and ignorance ("unknown unknowns"), it may prove an impossible task to inform affected persons adequately.

Safety issues

At the nanoscale size, materials exhibit very different properties from materials of the same composition at a larger scale. Strength, conductivity, color and toxicity all change at the nanoscale and properties can change within the nanoscale as well. Although the widespread use of nanotechnology is just beginning, concerns are raised relating to the safety aspects [2]. Nano particles have a large surface area volume ratio. The greater the specific surface area, the more chance it could lead to increased rate of absorption through the skin, lungs or digestive tract. This could cause unwanted effects in the lungs and other organs throughout the body, as non-degradable nanoparticles could accumulate. Most nanosized spherical solid materials could easily enter the lungs and reach the alveoli [37]. This primary toxic effect is respiratory tract inflammation, causing tissue damage and subsequent systemic effects [38]. Penetration via skin might facilitate the production of reactive molecules that could lead to cell damage.Transport through the blood stream to other vital organs or tissues may result into other systematic effects [39].

Despite the numerous health and healthcare advances provided by nanomaterials and nanotechnologies, several side effects have also been noted. The main health risks related to the use of such devices consist of cytotoxicity, translocation to undesired cells, acute and chronic toxicity, unpredictable and indeterminate safety concerns, and the environmental impact of nanomaterials and nonbiocompatibility. Some nanoparticles show increased toxicity due to their increased surface area [40]. Studies have shown carbon nanotubes to be cytotoxic and to induce granulomas in the lungs of laboratory animals. Also, metals and metallic oxide nanoparticles such as copper, cobalt, titanium oxide, and silicon oxide have inflammatory and toxic effects on cells [41]. There is an ongoing debate among researchers about the benefits and risks of nanotechnology. There are no exact Food and Drug Administration (FDA) regulations for the control of nanotechnology-based materials and allied problems. Overall, there is a critical requirement to standardize these nanotechnology-based products and delivery devices. Characterization, safety, and environmental impact are the three main elements that need to be regulated. However, regulatory agencies are regulating the major health risks associated with nanomaterials. Workers may be exposed to nanosized particles in the manufacturing or industrial use of nanomaterials.

CONCLUSION

The benefits of nanotechnology are enormous, therefore studies that examine the health, environmental, ethical, and safety issues should improve our understanding of how to exploit the benefits and diminish the risks. In view of the fact that many nanomaterial, new or miniaturized bulk particles are ready to enter the market, it is probably wise that authorities and legislators support fundamental research to construct a scientifically valid, low-cost, fast-throughput toxicity test battery to screen non-material for toxicity and bio persistence.

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