AN INSIGHT INTO THE APPLICATIONS OF NANOTECHNOLOGY AND STEM CELLS IN PROSTHODONTICS-A REVIEW

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ABSTRACT

Nanostructure is the one with dimensions less than 100nm and these have been found to influence the chemical and physical properties of the larger materials. Stem cells are undifferentiated cells that differentiate into specialised cells. Nanomaterials have been rapidly developed, and some prosthodontic research has been done using them. Many of the dental materials used today have nanotechnology incorporated into them to enhance their characteristics and, in turn, their original performance. An effective long-term therapy option for replacing missing teeth is dental implants. Implant implantation presents challenges in highly resorbed bone. This can necessitate other surgical operations, such bone augmentation. Technology advancements in stem cell and bio-engineering offer solutions to replace missing hard and soft tissues for implant placement. Stem cells and nanomaterials may become the best resource for prosthodontic regenerative medicine and in dental material science with the advancement of scientific and clinical research.

KEY WORDS: Nanomaterials, Scaffolds, Stem Cell types, Differentiation, Tissue regeneration, Implants.

INTRODUCTION

Nanotechnolog is "the creation of functional materials, devices, and systems through control of matter on the nanometer scale, i.e., 1–100 nm, and exploitation of novel phenomena and properties, such as physical, chemical, and biological at that length scale." Understanding and manipulating matter at the nanoscale, or dimensions between one and one hundred nanometers, is known as nanotechnology. This phenomena enables a variety of unique uses. The use of nanomaterials is included in nanotechnology. Natural materials, incidental materials, or produced materials that consists of particles in free state, as agglomerate/ aggregates where at least

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fifty percentage of particles are distributed between 1 nm and 100 nm sizes is referred to as a nanomaterial.[27,42]

Nanomaterials could be categorised as nanomembrane, nanofiber, nanopowder, nanoblock, in where nanopowder development has been higher[47] Nanomaterials are smaller but with large surface area and surface energy. They also posses large surface atom proportion, and the following effects:effect of small size, effect of quantum size, effect of quantum tunneling, and that of surface.[27]

Nanotechnology has emerged in to two new fields, that are nanomedicine and nanodentistry. Nanodentistry with the use of nanomaterials aids in maintaining comprehensive oral health[11]. With the aid of the nanotechnology concept, a variety of physical and mechanical qualities of dental materials can be changed and improved. Nanomaterials are being created at a faster rate, and some study on them is being done in the prosthodontics sector as well[58].

Undifferentiated totipotent cells, known as stem cells differentiate into any form of cell. They are ideal cells for manipulation in vitro because they maintain good viability and exhibit stable division. Current medical applications of stem cell technology include the treatment of type 1 diabetes[19], tendon ruptures, heart failure[29], spinal cord damage, and retinal and macular degeneration[49] and type 1 diabetes[19].

In dentistry the application of stem cells is a newer phenomenon that may find its wide application in the field of regenerative dentistry. In the field of prosthodontics application of stem cell technology is majorly concentrated in the field of bone regeneration.

NANOPARTICELS CATEGORIES:

1. Nano rods(10 - 120 nm). Enamel-prism like hydroxyapatite nanorods
2. Nano wires(10 nm)
3. Nano tubes; the dimensions are expressed in terms of ratio (length / width)-single/multi-walled tubes.
4. Nano powders: powdered materials with individual particles in nanometer scale.

PRODUCTION OF NANO PARTICLES:

The fabrication techniques of nanomaterials has two approaches.

1) Top-Down approach: By further shrinking into nano sizes, this strategy produces nanoscale structures based on techniques already used in small-scale assembly at the micro scale levels. Examples of top-down approaches include nanocomposites, bone graft materials, impression materials, nanosolutions, nanoencapsulations, and nanoneedles.

2) Bottom-Up approach[30]: This method creates nanomaterials using techniques utilised just to create nanoscale objects. Local anaesthetic, nanorobotic dentifrice, treatment for hypersensitivity, orthodontics, dental cosmetics, photosensitizers and carriers, and the detection and management of oral cancer are some of the examples of bottom-up approaches.

APPLICATIONS OF NANOTECHNOLOGY IN PROSTHODONTICS:

1.Nanoceramics:[20]

In the microstructure phase, nanoceramics are ceramic materials with nanoscale dimensions. In comparison to traditional ceramics, nanoceramics are more flexible and stronger. Superior mechanical qualities like improved strength and hardness are present in them. Durability of nanoceramics is higher than that of conventional ceramics. Nanoceramics have 4-5 times higher strength and hardness than conventional materials. Carbon nanotubes (CNTs) have higher electrical and material properties.

2. Nano resin materials:[20]

Nano resin materials can be nanohybrid materials and nanofilled materials. The non-agglomerated, nanoparticles—nanomers and nanoclusters—which are uniformly disseminated in resins create nano composites. To increase the powder flow of composites, little amounts (1%–5%) of nanomaterials such as titanium dioxide, silicaoxide are utilised. Newer light-cure nano composites are produced by the addition of nano fillers to resin matrix and offer enhanced mechanical strength, equivalent wear resistance, superior flexural strength, higher translucency, superior elastic modulus, Superior polish and gloss resistance in comparison to microfilled-composites[5]

3.Materials used for impressions:[4]

Impression material refers to any substance or mixture that is used to create a negative impression or reproduction. The capacity to replicate tissue surface, record details properly are of the utmost importance to make a dental prostheses with no corrections. In order to moisten the hard tissues and soft tissues of the lips and to create an accurate impression, the hydrophilicity of the impression materials and for precise castings and impressions to be made of hard tissues, soft tissues of oral cavity, hydrophilicity of impression materials is absolutely essential. Despite the fact that poly vinyl siloxanes (PVS) are naturally hydrophobic, adding nanofillers, such as silica nanofillers processed in a top-down manner, to PVS results in a material with improved flow, hydrophilic properties, fewer voids in the margins, and

better model pouring with more accurate and precise detail placement.[28,44]

4. Tissue conditioner:[4]

These have been widely utilised in aiding healing of denture-bearing tissues after injury, that is typically brought on by ill-fitting dentures. Mechanical and chemical cleaning techniques might be used to maintain tissue conditioners, but doing so could seriously harm them[14,40.] The antibacterial properties of silver are well recognised[39]. Because of their tiny size and surface area being higher, silver nanoparticles are added to tissue conditioners to solve this issue.

5. Nano composite teeth:[4]

The invention of resin-based composite technology has been one of the significant achievements in dentistry. For both anterior and posterior restorations, they have largely dominated the field of cosmetic dentistry[31].The application of dental composite in restorative procedures still faces certain difficult challenges, including polymerization shrinkage and low strength. Over past few years, researchers were investigating the development of dental composite resins with low shrinkage. The lack of clinically applicable mechanical qualities of low shrinkage dental composites is a significant barrier to their development. New restorative materials have been developed as a result of the desire for aesthetic restorations that are more enhanced. In the recent past, restorative nanocomposites made of nanofillers have become very popular. Materials with superior adhesive, cosmetic, and mechanical qualities compared to earlier composites (Nano fillers differ significantly from conventional fillers and call for a change in production strategy from top-down to bottom-up). There are two types of nano filler particles: individual nanomeric particles and clusters of nanoparticles.

Both methods can produce a good composite, but the nanohybrid method may still be hampered by the loss of larger particles and a possible reduction in initial gloss[23]. Using organo-silane-triethoxy-siloxane (ATES)-treated titanium dioxide nanoparticles, composites' micro-hardness and flexural strength have been increased[59].

6. Polymethyl methacrylate resin:[20]

Biofilm adhesion to denture base is the primary cause of oral pathological conditions such denture stomatitis. As an efficient antibacterial agent, Ag and Pt nanoparticles are primarily used into denture base materials. According to certain studies, adding metal nanoparticles to PMMA materials, such as TiO2, Fe2O3, and silver, can rise the surface

hydrophobicity and decrease bimolecular adhesion. The viscoelastic qualities of the acrylic denture base material may be improved by the addition of AgNPs. To increase the function of PMMA, several nanoparticles including zirconium oxide, titanium dioxide, and carbon nanotubes (CNT) are utilised. The mechanical properties of heat-cure monomer have been improved and polymerization shrinkage has been minimised by the use of carbon nanotubes. The flexural strength, antibacterial activity, and reduced porosity of standard polymethyl methacrylate have all been enhanced by the addition of metal oxide nanoparticles.

7. Adhesives:[4]

Dental adhesives are chemicals that are used to encourage cohesion or adhesion between two unlike materials or that between a material and natural tooth. Dental adhesives have silane that can be polymerised to improve cohesive strength. The filler particles have a tendency to settle during storage. Dental adhesives are supplemented with silane-treated nanoparticles of Zr or Si with (5-7 nm)[24] to solve this drawback. Dental adhesives' binding strength did not decrease following the addition of Si or Zr nanoparticles according to studies[51].

8. Coating agents in prosthodontics:[4]

Prosthodontic coating agents are used over glass ionomer restorations, composite restorations, veneers, jacket crowns, provisionals. They are light cured and contain nanosized fillers. According to Abiodun-Solanke[1], these coating agents offer greater wear resistance and guard against abrasion and discoloration.

9. Implants:[20]

Nanoparticles can be coated on top of dental implants to incorporate nanotechnology into them. It has been shown that several cell types react favourably to nano coated topography. The close integration of the implant's nanocoated surface with surrounding bone is crucial in determining biocompatibility and biointegration. The important material parameters affecting bone-implant contact are implant surface composition, energy, roughness, and topography. Biomimetic implant could be the future advancement. Along with cell differentiation and proliferation , promoting higher vascularity in cortical bone; using implant coatings made of nano-textured titanium, Hydroxyapattite (HA), and pharmaceuticals like bisphosphonates may improve the circumstances for remodelling of bones in short and long-term. It is a potent method of changing how proteins interact with surfaces. When compared to conventional surfaces, the adsorption of

vitronectin is increased on nanostructured surfaces.

10. Bone augmentation materials:[20]

Bone naturally has nanohydroxyapatite (HA), with collagen fibrils the interaction of which influences the strength and toughness of the bone. The apatite crystals can mechanically stabilise the collagenous fibres, the fibrous collagen matrix can transfers load to apatite crystals and offer fracture resistance. Nanohydroxyapatite(HA are commercially available) and are used for bone augmentation.

11. Maxillofacial prosthodontics:[4]

Silicone is the most commomly used extra-oral maxillofacial material. Its texture is similar to human skin. It is flexible. But its limitations include reduced clinical longevity of the prosthesis, instability of colour and deterioration of material with time. To overcome this nanoparticles such as Ti, Ce, Zn, $BaSO_4$ were incorporated that enhanced physical properties of silicone material.

STEM CELLS TYPES:

A. Embryonic stem cells:These are obtained from blastocysts, which are supernumerary embryos that are 2–11 days old, at in vitro fertilisation facilities. These cells, or germ cells, are totipotent. ESCs can exist in an undifferentiated condition and continue to grow indefinitely. They are thought to have the greatest capacity to regenerate and mend damaged tissues. There are moral and ethical issues with deriving ESCs . Additionally, controling the differentiation, expansion of ESCs is difficult, which increases the likelihood of teratoma development and tumorogenicity. While there is currently research underway to address some of these deficiencies, ESCs have not yet been used therapeutically and have instead served as a good research platform.[48]

B.Adult Stem Cells:These are undifferentiated cells can be found in tissues that have undergone tissue differentiation. These can be found in the following tissues: bone marrow, brain tissues, in blood, eyes, skeletal muscle tissues,digestive tract lining, pancreas, tooth pulp, and skin tissue. ASCs have multipotent property located at regions known as niches. The cellular environment that these Niches offer is specialised to self-regeneration. Tissue stem cells are adult stem cells located other than the bone marrow. ASCs multiply to replace degenerating cells and repair damaged tissue. When produced in culture, ASCs are challenging to distinguish, purify, and keep in an undifferentiated condition.[2,25]

Among most practical sources of stem cells is bone marrow from the iliac crest.

By using flow cytometric surface marker sorting[34], Okano and colleagues were able to identify BMSC populations that were highly pure and proliferative. The formation of the cranium, face bones, and oral mesenchyme are embryologically connected, and these pure BMSCs displayed a phenotype similar to neural crest cells[38]. Given their embryonic origin, mesenchymal stem cells (MSCs) which are similar to cranial neural crest cells may be useful for craniofacial regenerative medicine. Mesenchymal stem cells (MSCs) have regeneration capabilities that are site-specific which may depend on source and type of MSCs

Another interesting cell source is induced pluripotent stem cells (iPSCs), which can perhaps develop into bone and dental cells. By creating transplantable iPSC-based biomimetic bone in vitro, Egusa and colleagues[40] created 3D bone tissue-like cell constructions from iPSCs of mouse. This work may pave the way for new technologies.

DENTAL STEM CELLS:

They can be mesenchymal and epithelial stem cells:

A. Dental mesenchymal stem cells:

The dental pulp of permanent human teeth was where dental mesenchymal stem cells (DMSCs) were initially discovered[12,13]. Additionally, dental pulp tissue from deciduous teeth that is exfoliayed[32], the apical portion of dental papilla[52], the dental follicle[35], and the periodontal ligament are all places where DMSCs have been isolated.

DPSCs, or dental pulp stem cells: Pulp tissue from 3rd molars is the most frequent source of DMSCs. In vitro, they can develop into the lineages odontogenic[12,13,32], adipogenic[13], chondrogenic[56], osteogenic[7], myogenic[22], and neurogenic[13].

A.2. Apical stem cells from the papilla (SCAPs), which are extracted from tissue at the apex of permanent teeth which is developing[52]. These have increased proliferation rate and increased telomerase activity as compared to DPSCs[52]

A.3. Periodontal ligament stem cells (PDLSCs) were originally isolated from 3rd molars by severing the periodontal ligament (PDL) from the root surface (rPDLSCs)[50]. Under specific in vitro circumstances, rPDLSCs can develop into adipogenic and osteogenic cells[10].Alveolar periodontal ligament stem cells (aPDLSCs), a different population of periodontal stem cells, have recently been discovered adjacent to the alveolar bone. As compared to rPDLSCs, aPDLSCs had much stronger osteogenic and adipogenic potential[57].

A.4. Dental follicular stem cells (DFSCs): These exhibit in vitro potentials for both osteogenic and cementogenic properties.Dental epithelial stem cells (EpSCs),originate from inner enamel epithelium and then develop into ameloblasts to form tooth enamel.These are obtained from third molars or the malassez epithelial cell rests.

PROSTHODONTIC APPLICATIONS OF STEM CELLS:

1) Regeneration of adult teeth: Stem cells and tissue engineering will one day make it possible to regenerate adult teeth. According to studies, tissue engineering technology can help rebuild the tooth's crown. Inductive morphogenesis is the process of tooth regeneration. Adult stem cells are extracted and sown into a scaffold during this technique. These cells receive spatial instructions from molecules.

In their investigations, Duailibi et al.[9] demonstrated that it is possible to grow teeth from suspensions of cultured tooth bud cells of rats. In 12 weeks, tissue-engineered teeth of rat were produced on a PLGA and PGA scaffold. Young et al.,[60] created a crossbreed tooth bone for the treatment of loss of tooth in addition to alveolar bone resorption utilising porcine tooth bud cells, PLGA, and PGA scaffolds[9,17,36,37,60].

2. Alveolar bone regeneration: The process of developing bone requires MSCs aggregating into mesenchymal condensations, which is nearly identical to the process of developing teeth without the invagination of epithelium. MSCs taken orally appear to be the best choice for bone repair.

3. Craniofacial regeneration: Stem cell therapy was used in a randomised, controlled human experiment to regenerate craniofacial bone. Results showed that cell therapy at treatment locations accelerated the regenerative response on clinical, radiographic, and histological levels. Additionally, there was a much lower need for subsequent bone grafting surgeries.[45.]

4. Periodontal regeneration: According to Kawaguchi et al. ex vivo prolonged autologous MSC transplantation may regenerate new periodontal ligament, cementum, and alveolar bone in periodontal deficit(class III) in dogs.[48].

STEMCELLS AND NANOTECHNOLOGY IN PROSTHODONTICS:

NANOSCAFFOLDS:

The scaffolds' nanofibers serve as anchors for the stem cells, which are then transferred to the surgery or lesion site. This will increase stem cells' chances of surviving, migrating, and differentiating, as well as their capacity for 3D

organization[33]. When compared to stem cells produced on standard substrates, nanofiber scaffold-grown stem cells have higher vitality, less motility, and a different morphology[26]. Nanofiber scaffolds have a unique surface with significant porosity, which provides the perfect environment/place for stem cell growth. The creation of tissue-specific artificial niches opens up new possibilities for the use of stem cells to treat abnormal anatomical sites (such as the long bones, alveolar bone, teeth, periodontium, heart, and muscles). This technique has been successfully used in regenerative medicine[15,16].

NANOTECHNOLOGY FOR DESIGN OF ARTIFICIAL STEM CELL NIC:

The improvement of adherence, osteogenic differentiation, growth and alignment of the mesenchymal stem cells has been demonstrated on irregular surfaces of nano polymethyl methacrylate[6,8], These findings show that such nanomaterials can be applied to the creation of new nanotextured "osteogenic coating" dental implants, resulting in better osteogenesis.

CONCLUSION:

Various advances in the field of nanotechnology such as improvement in material properties by incorporating nanomaterials, bioprinting incorporating stem cells and nano materials and advancement of nanobots and those in stem cell therapy and bio-engineering such as regeneration of the tissues and tissue healing and their applications in the field of prosthodontics has been shown to improve treatment care. More research and studies are needed in nanotechnology and stem cells therapy to open up various new prospects in the field of prosthodontics that might revolutionize the direction of prosthodontic rehabilitation.

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