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# A Concise Overview of Biomaterials and the Diverse Uses of Nano Hydroxyapatite across Different Fields

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**ABSTRACT:**
Bruck (1900) defined biomaterials as substances, whether synthetic or natural, designed for use in prosthetic, diagnostic, therapeutic, and storage applications involving contact with tissue, blood, and biological fluids. They must not harm living organisms or their components. Biomaterials interact with tissues and bodily fluids over extended periods. They fall into two main categories: natural biomaterials sourced from plants or animals, which can enhance, replace, or restore biological tissues with properties like in-vivo immunomodulation, detoxification, and biomimicry (e.g., proteins, gelatin, alginate, silk, fibrin, cellulose, chitin, chitosan); and synthetic biomaterials, manufactured in laboratories or industries by human effort (e.g., metals, ceramics, polymers). Natural and synthetic biomaterials notably differ in their ability to provoke host responses upon implantation, including inflammation, matrix formation, blood interactions, and the development of granulation or fibrous capsules.

**Keywords**: Biomaterials, hydroxyapatite, Biocompatible, Orthopedic**,** osteoblast, biodegradation.

## 1.1 INTRODUCTION

Using nanomaterials as biomaterials offers significant advantages over their microstructured counterparts. When materials are reduced to the nano scale, they exhibit extraordinary chemical and physical properties, accompanied by a substantial increase in surface area relative to volume. Nanophase biomaterials, due to their larger surface area, are more responsive to surrounding growing cells. Additionally, these materials create a complex biological environment at the nano level, incorporating extracellular matrix proteins (ECM), which support cell survival, organization, and proliferation. This approach is pivotal in developing nanophase biomaterials aimed at healing and regenerating damaged tissues. Compared to traditional biomaterials, nano biomaterials facilitate faster tissue reconstruction.

## 1.2 BIOMATERIAL CLASSIFICATION BASED ON CHEMICAL BONDING

Synthetic biomaterials vary in their bonding characteristics (covalent, ionic, or metallic) and properties, influencing their specific applications within the body. Each material has distinct advantages and drawbacks, dictating its biomedical uses based on its unique features and intended site of application. Figure 1.1 illustrates the classification of key synthetic biomaterials.

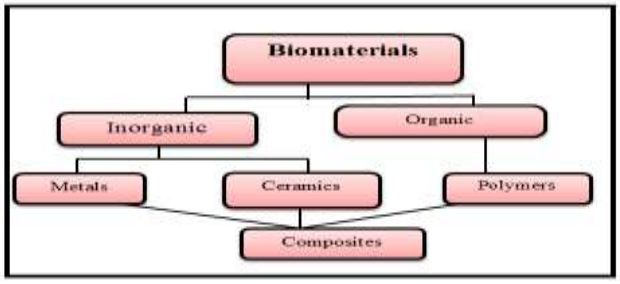


**Figure 1.1 Classifications of biomaterial**

### 1.2.1 Metallic Biomaterials

Metallic biomaterials, including alloys used in medical devices, have been employed in dentistry for over 80 years and have found applications in spinal, cardiovascular, orthopedic, and other medical fields since 1960s. These materials are primarily used for load-bearing applications and must possess sufficient fatigue strength to endure the stresses of daily activities. The three most commonly used implantation metals are titanium-based alloys, 316L stainless steel, and cobalt-chromium-based alloys. Additionally, metals such as gold, tantalum, dental silver fillings, and other specialty metals are utilized in biological applications. Chromium and its alloys are used for manufacturing heart valves, while magnesium and its alloys are employed to create biodegradable metallic stents. Nitinol alloys (nickel-titanium alloys) are ideal for cardiac implant devices. Silver is used as a coating agent in implant devices due to its anti-inflammatory and infection-suppressive properties. Titanium and its alloys are used to encase pacemakers. Metals are technologically intriguing because their properties can be modified in a more extensive and adaptable manner than polymeric materials and ceramics, depending on the manufacturing processes used. [1]. Table.1.1 gives the advantages, disadvantages and applications of metallic biomaterials.While most metallic implant materials are biocompatible, they can still release ions. For example, stainless steel implants may gradually release $Cr^{3+}$, $Ni^{2+}$, and $Cr^{6+}$ ions into the body over time, which restricts their use in long-term devices.

**Table 1.1 Advantages, disadvantages and applications of metallic biomaterials**

### 1.2.2 Polymeric Biomaterials

| Metallic Biomaterials | | |
|---|---|---|
| **Advantages** | **Disadvantages** | **Applications** |
| ➢ High Strength<br>➢ Resistance to wear<br>➢ Resistance to fatigue<br>➢ Good ductility.<br>➢ Excellent electrical and mechanical property.<br>➢ Simple to make.<br>➢ Possess shape memory effect.<br>➢ Sterilization is simple. | ➢ Corrosive<br>➢ High modulus of elasticity<br>➢ Metal ion toxicity and sensitivity<br>➢ Stress shielding<br>➢ Osteolysis | ➢ Artificial joints, plates and screws.<br>➢ Braces and dental implants.<br>➢ Artificial heart, staples, stents, wires and coils.<br>➢ Vascular grafts |

Polymers play a vital role in tissue engineering and can be used for varying durations in physiological conditions. These biomaterials are classified as either natural or synthetic, based on their origin [2].

Disposable medical devices like catheters, syringes, and blood bags are typically made from synthetic polymers. Non-resorbable synthetic polymers are used in orthopedic implants, vascular grafts, long-term drug delivery systems, barrier membranes, tissue engineering, and blood-contacting devices. Synthetic resorbable polymers are utilized in applications such as artificial skin, wound dressings, orthopedic implants, and tissue engineering. When selecting a polymer for use as an implant biomaterial, it is essential to match its the surrounding tissue heals [3]. Biodegradable polymers have been created specifically for medical use within the body. The main advantage of degradable polymer implants is that they eliminate the need for a second surgery. However, the primary disadvantage is their potential to release toxic acids and other pollutants during the degradation process. Examples of polymeric biomaterials include Nylon, Polyethylene, silicone, Teflon, Dacron, acrylates, polyglycolic acid (PGA), polylactic acid (PLA), and ultrahigh molecular weight polyethylene (UHMWPE). Hydrogels are another type of polymer that has garnered significant interest due to their biological applications. These three-dimensional, cross-linked polymer network structures are water-insoluble and can retain large amounts of water. They swell when absorbing water and have the ability to polymerize under physiological conditions in vivo. Hydrogels are used in contact lenses, hygiene products, and wound dressings. Additionally, they can serve as fillers, carriers for bioactive drug delivery, and 3D structures that support cells and facilitate the development of ideal tissue. The advantages, disadvantages and applications of polymeric biomaterials are shown in Table.1.2.

**Table 1.2 Advantages, disadvantages and applications of polymeric biomaterials**

| Polymeric Biomaterials | | |
|---|---|---|
| **Advantages** | **Disadvantages** | **Applications** |
| ➢ Resilent<br>➢ Easy to fabricate.<br>➢ Flexible.<br>➢ Bio degradable.<br>➢ Better mechanical property and structural stability | ➢ Excessive elastic modulus.<br>➢ With time, it deforms.<br>➢ Hard to sterilize.<br>➢ Absorb water and protein | ➢ use in dentistry (Prosthetic implants, Filling materials).<br>➢ General and cardiovascular surgery: Implants (vascular graft, pacemakers, artificial heart and heart valves).<br>➢ Controlled release of drugs. |

### 1.2.3 Composite Biomaterials

In many medical applications, metal, polymer, or ceramic alone may not provide all the necessary properties. Composites are created to overcome some of these limitations. Composites are engineered materials consisting of two or more component elements with significantly different chemical, physical, and mechanical characteristics. The components do not completely merge or lose their individual identities; instead, they combine to impart their most beneficial qualities, resulting in enhanced strength, efficiency, and durability of the final product. A composite is formed by combining two phases: a continuous phase (matrix) and a discrete (reinforcing) phase. The reinforcing phase consists of particles, fibers, and sheets embedded in the matrix. Properly designed composite biomaterials can be used as direct replacements or integral functionalities for organs damaged by traumatic or pathological events [4]. Composite biomaterials are categorized based on their constituents into fiber-reinforced, particle-reinforced, and structural types. Polymers, ceramics, metals, and carbon serve as matrix materials in var-

ious composites.

Polysulfone (PSU) and Polyether ether ketone (PEEK) are high-strength polymers that provide a robust matrix for composites. Consequently, these materials are combined with hydroxyapatite to create HAp/PSU and HAp/PEEK composites for bone tissue repair. The metal matrix composite (HA/Ti-6Al-4V) is used for heavy load-bearing applications. Biodegradable composites are designed to act as bioactive matrices, supporting and guiding tissue development. Synthetic biodegradable polymers such as poly glycolide (PGA), poly lactide (PLA), and polycaprolactone (PCL) are used as matrices, while bioactive bioceramics like hydroxyapatite (HAp) and tricalcium phosphate (TCP) serve as dispersion phases for targeted applications. CF/PEEK is a bioinert composite with mechanical properties similar to metallic materials, used for internal fixation. The advantages, disadvantages and applications of composite materials are given in Table.1.3.

**Table 1.3 Advantages, disadvantages and applications of composite biomaterials**

| Composite Biomaterials | | |
|---|---|---|
| **Advantages** | **Disadvantages** | **Applications** |
| ➢ optimal stiffness and strength<br>➢ Better fatigue life.<br>➢ Less weight<br>➢ Resistance to corrosion.<br>➢ In mild to medium repairs, it has a long life span. | ➢ Expensive<br>➢ Difficult to fabricate.<br>➢ If correctly bonded, leakage is minimal. | ➢ Tissue Engineering<br>➢ Drug delivery.<br>➢ Wound healing.<br>➢ Bio implant<br>➢ Biosensor. |

### 1.2.4 Ceramic Biomaterials

Also known as bioceramics, these non-metallic inorganic solids are created by heating followed by cooling. They can have crystalline, partially crystalline, or amorphous structures. Due to their covalent and ionic bonding, ceramics are typically refractory materials capable of withstanding high temperatures. These materials mimic the properties of bone and, when used as bone implants, can induce bone growth. Ceramic biomaterials that establish good interfaces with bones, which are biologically significant, can promote strong bone adhesion. As they degrade, the surrounding tissues remain unaffected. Ceramics have a low friction coefficient, ranging from 0.2 to 0.8, and possess a higher hardness value than steel, typically between 10 and 30 GPa [5]. These materials encompass zirconia, alumina, bioactive glasses, calcium phosphate, and other glass ceramics. The advent of bioceramic implants manufactured at the nanoscale has transformed their application in orthopedic surgery. Table.1.4 gives the advantages, disadvantages and applications of ceramic bio materials.

**Table 1.4 Advantages, disadvantages and applications of ceramic biomaterials**

| Ceramic Biomaterials | | |
|---|---|---|
| **Advantages** | **Disadvantages** | **Applications** |

| | | |
|---|---|---|
| ➢ Biocompatible<br>➢ Better tissue responding property.<br>➢ Withstand high temperature<br>➢ Excellent compressive strength and load bearing capacity.<br>➢ Bone bonding ability. | ➢ Low toughness<br>➢ In elastic<br>➢ Difficult to synthesize.<br>➢ Brittle<br>➢ High modulus (not matched with bones)<br>➢ Low tensile strength | ➢ Orthopaedic and dental implants.<br>➢ Diagnostic instruments.<br>➢ Bone graft substitutes.<br>➢ Bone cements.<br>➢ Hip prosthesis<br>➢ Heart valves<br>➢ Artificial tendons and ligaments<br>➢ Artificial joints |

### 1.3 KINDS OF BIOCERAMICS

Bio ceramics are classified into inert, resorbable and bioactive ceramics (Figure.1.2). Bio-inert ceramics that are compatible with the physiological environment and do not interact with surrounding tissues. These materials possess desirable implant qualities such as corrosion resistance, low inflammatory response, non-toxicity, and non-allergenicity. Advances in nanotechnology have enhanced the physical, chemical, biological, and mechanical properties of these inert ceramics. Resorbable ceramics are chemically broken down and degraded by the body, but this degradation results in a significant reduction in mechanical strength. The biological response of these degradable bioceramics is influenced by their physical and chemical structure. A key challenge in developing these bioceramics is maintaining the stability and strength of the interface during degradation. Bioactive ceramics form a chemical bond with surrounding tissues through ion exchange. This category of bioactive ceramics includes glass ceramics and calcium phosphate ceramics.

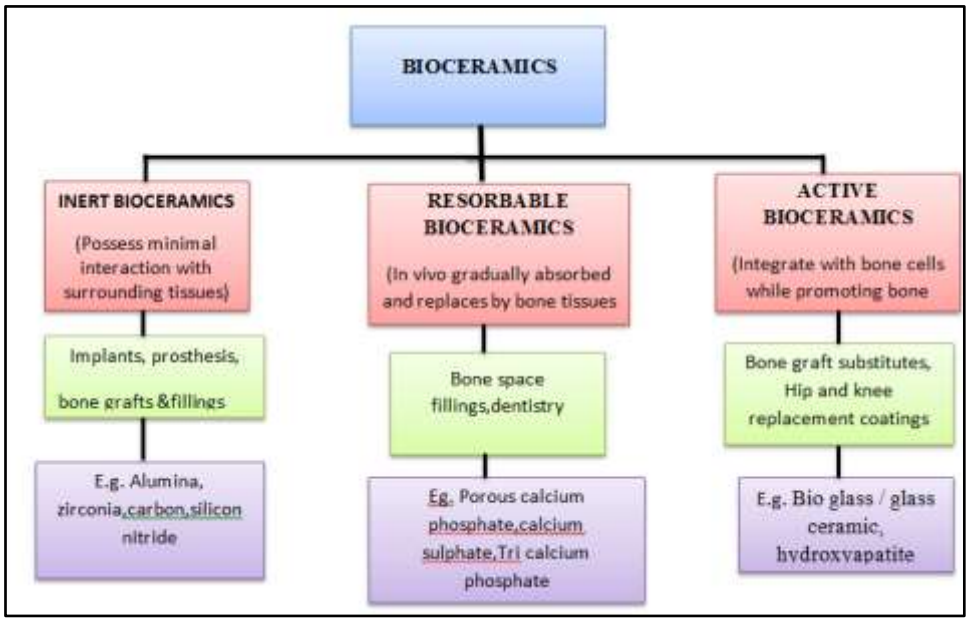


**Figure 1.2 Classification of bioceramics**

Calcium phosphates are a crucial inorganic mineral component of biological hard tissues, making them one of the most significant bioceramic materials. The discovery of calcium phosphate in bone tissue in 1769 marked a major milestone in medical history. Since then, scientists have concentrated on calcium phosphate ceramics for treating dental and bone issues. Various forms of calcium phosphates exist, each differing in composition due to variations in their production processes and origins. These calcium phosphates are present in different parts of the body, including dentine, enamel, bone, urinary stones, and soft tissue calcifications. Table.1.5 provides information on the various calcium phosphate phases based on their Ca/P ratio.

## 1.4 HYDROXYAPATITE

Hydroxyapatite is the most important calcium phosphate-based bioceramic, recognized for its bioactivity and stability. It closely resembles the mineral components of hard tissues in its chemical composition. The term "apatite" denotes a group of phosphate minerals with the general formula M10(XO4)6Z2. In this formula, M2+ represents metallic elements, while XO43- and Z are anions [6]. Each apatite has a distinct name depending on the M, X, and Z groups. In the case of hydroxyapatite, M stands for calcium ($Ca^{2+}$), X stands for phosphorus ($P^{5+}$), and Z stands for hydroxyl ($OH^-$) ions The chemical formula of hydroxyapatite is $Ca_5 (PO_4)_5(OH)$. To show the two entities of a unit cell, the formula is usually written as $Ca_{10} (PO_4)_6(OH)_2$. The weight percentages of each element in HAp are as follows: calcium (39%), phosphorous (18.5%), and hydroxyl (3.38%) [7]. The atomic ratio of calcium and phosphorus in hydroxyapatite is 1.67.

## 1.5 OCCURRENCE OF HYDROXYAPATITE IN THE BODY

Hydroxyapatite is a key and essential component of teeth and bone. It is widely recognized that synthesized hydroxyapatite closely resembles the mineralized tissues of mammals, such as teeth and bone.

### 1.5.1 Teeth

Teeth are composed of four components: enamel, dentin, pulp, and cementum (Figure.1.3). Enamel forms a thin outer layer on the tooth and is the most highly calcified and toughest tissue in the human body. It contains 97 wt% hydroxyapatite crystals, which have lengths ranging from 160 to 1000 nanometers, thicknesses of 25 nanometers, and widths of 40 to 120 nanometers. Most of the crystallites have a hexagonal cross-section. The remaining 3 wt% of enamel consists of fluoride, strontium, magnesium, and water. Below the enamel is the dentin, which is softer and more vascularized than the enamel. In addition to supporting the enamel, it connects the tooth's pulp to the crown through a complex tubular structure. Dentin contains 70 wt% hydroxyapatite, found in the spaces between collagen fibrils, similar to the composition in human bone. It is entirely covered by tooth cementum. Although dentin has the lowest hydroxyapatite concentration among mineralized tissues, it has the highest fluoride content. The pulp, the innermost part of the tooth, is directly connected to nerves and blood vessels and consists entirely of connective tissues.

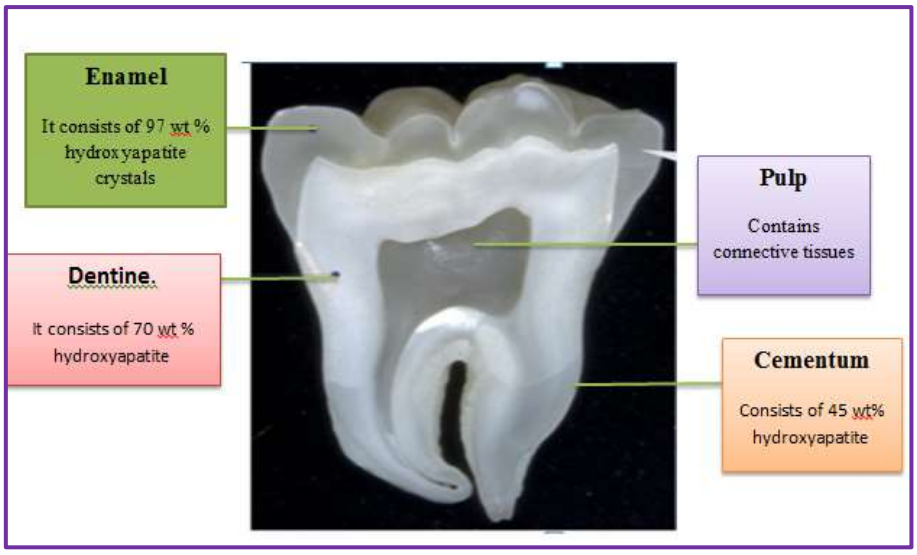


**Figure 1.3 Parts of a tooth**

### 1.5.2 Bone

Bone is the essential structural component of the human skeleton. It is a mineralized, highly vascular connective tissue comprised of cells and a dense organic matrix that is infused with inorganic salts. . The bone matrix is the portion of the bone tissue that makes up the majority of the bone's bulk. As shown in Figure.1.4 (a) the bone matrix consists of 33% organic matter, mainly Type I collagen along with a small amount of ground substances, and 67% inorganic matter, predominantly calcium phosphate in the form of hydroxyapatite crystals. These inorganic hydroxyapatite crystals are embedded within the organic matrix of collagen fibers and other proteins[8] as shown in Figure.1.4 (b).

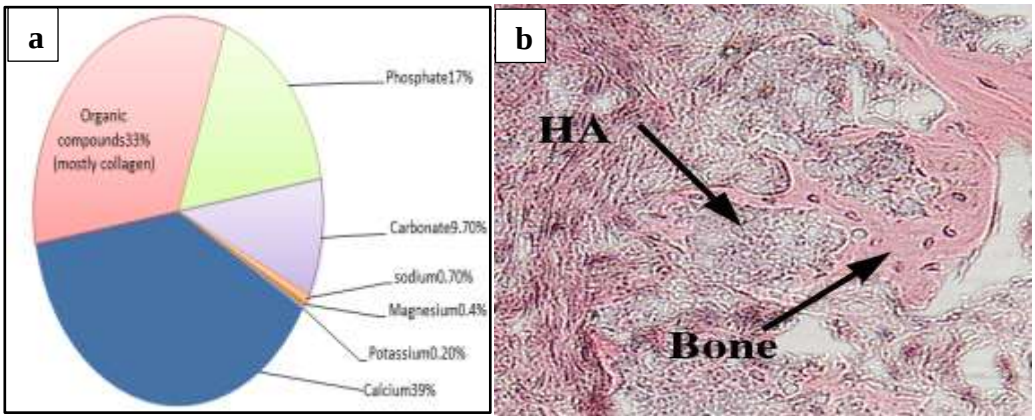


**Figure 1.4 (a) Chemical composition of bone (b) HAp embedded in bone matrix**

Organic collagen is a triple-helix protein made up of one alpha-2 and two alpha-1 polypeptide chains, found throughout the human body. In bones, it forms a framework that facilitates mineralization, which enhances the mechanical stiffness, tensile strength, and stress resistance of bone. Alongside type-1 collagen, the organic bone matrix also contains small amounts of other collagens, glycoproteins, and non-collagenous proteins. Although the exact role of these non-collagenous proteins is not fully understood, they are thought to help in bone cell attachment to the matrix and regulate bone cell activity during remodeling.

The inorganic component of bone mineral consists of imperfect hydroxyapatite (HAp) crystals, which include impurities such as carbonate, sodium, magnesium, and potassium. These apatite crystals are needle-shaped, ranging from 40 to 60 nanometers in length, 20 nanometers in width, and 1.5 to 5 nanometers in thickness. Matured HAp nanocrystals have a plate-like shape, measuring 50 nm in length, 25 nm in breadth, and 2 to 3 nm in thickness. These crystals form in specific gaps within collagen fibrils, resulting in discrete and discontinuous crystals [9]. The HAp crystals align along the c-axis, which is parallel to the long axis of the collagen fibrils. Notably, the carbonate impurity replaces the phosphate group in hydroxyapatite, creating a carbonate apatite known as dahllite [10]. Other contaminants replace calcium ions in hydroxyapatite. These impurities reduce the crystallinity of apatite, which can impact its solubility. The solubility of bone mineral is crucial for mineral homeostasis and bone adaptation. HAp may increase local $Ca^{2+}$ levels, potentially promoting osteoblast proliferation and enhancing the development and differentiation of mesenchymal stem cells (MSC). The inorganic matrix of bone contributes to its stiffness and hardness.

## 1.6 SYNTHETIC HYDROXYAPATITE-ADVANTAGES AND DISADVANTAGES

Hydroxyapatite is the main mineral component of bone and teeth in the human body. Both biological (derived from marine algae, bovine sources, or coral) and synthetic hydroxyapatite are currently employed for bone regeneration and repair in various forms such as blocks, granules, and scaffolds. These can be used alone or combined with metals, polymers, or other ceramics, or as coatings on dental or orthopedic implants. Studies have demonstrated that synthesized hydroxyapatite can enhance the activity of osteoblasts (cells responsible for bone formation) and osteoclasts (cells that break down bone tissue) after implantation, compared to metallic or other ceramic biomaterials, thereby improving osseointegration (the integration of the implant with bone and soft tissue). As a result, synthesized hydroxyapatite is frequently utilized in dental and orthopedic applications, including dental prosthetics, periodontal treatment, alveolar margin augmentation, orthodontic surgery, and otolaryngology.

**Advantages**

It can integrate into bone structures and foster bone growth without collapsing or disintegrating.As a bioactive material, synthetic HAp enables bone to form a chemical bond with the implant directly, bypassing the need for a collagen interface layer. Hydroxyapatite is chemically unstable at high temperatures, degrading between 800 and 1200 degrees Celsius depending on its stoichiometry. Regarding biocompatibility, HAp is the most suitable ceramic material for implants used in hard tissue replacement. It is inherently non-toxic and non-inflammatory.

**Disadvantages**

The use of synthetic HAp is restricted in non-load bearing implants due to its inherent fragility, low tensile strength, and poor fracture resistance [11]. Another limitation is the non-degradability of pure HAp, which reduces its effectiveness under practical physiological conditions. The Young's modulus of synthetic dense HAp (5-15 x 10^6 psi) is higher than that of cortical bone (2 x 10^6 psi), indicating that it is more rigid than bone.

## 1.7 APPLICATIONS OF HYDROXYAPATITE

### 1.7.1 Orthopaedic and Dental Implant Coating

The HAp coating was designed to meet the most demanding biomechanical standards for bonding in high-stress orthopedic implants and intraoral treatments. Several methods are used to apply HAp

coatings to metallic implants. Since metal implants are often non-bioactive, HAp coatings can address this issue. The interface between the HAp coating and the surrounding tissue promotes new bone formation. The bioactivity of the HAp coating also supports the healing of damaged tissue. Additionally, the HAp coating serves as a protective layer against corrosion in aggressive bodily fluids and helps to slow the dissolution of metallic ions, thereby reducing the risk of leaching [12]. Literature indicates that hydroxyapatite and mineral compound composite coatings improve mechanical strength. The HAp/Chitosan film, in particular, is significantly stronger compared to a single HAp film. This is due to the active calcium silicate in the composite, which introduces porosity on the coated surface, enhancing its bioactivity and biocompatibility relative to a single HAp film [13]. Coating dental fixtures is essential for optimizing bone-implant contact. The use of HAp-coated implant surfaces significantly reduced the time needed for osseointegration of titanium implants by enhancing wettability and protein adsorption.

### 1.7.2 Gene and Drug Delivery

Gene delivery involves transferring foreign DNA into host cells for purposes such as gene therapy or genetic research. The main challenge in gene therapy is for the therapeutic gene to overcome extracellular and cellular barriers. A 'vector' is the carrier used to deliver the gene. There are two types of vectors: viral and non-viral. Viral vectors are effective at transfecting host cells but have significant drawbacks, including cytotoxicity and immunogenicity. Non-viral vectors, on the other hand, have lower pathogenicity, offering a safety advantage over viral vectors.

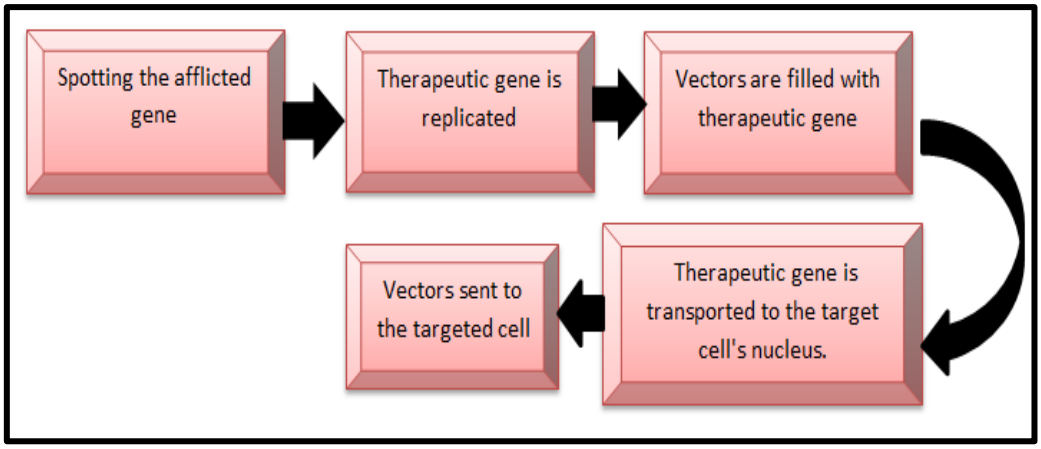


**Figure 1.5 Phases of gene therapy in stages**

Since the 1970s, HAp nanoparticles have been widely used as non-viral vectors. The negatively charged nucleic acids can bind strongly to CaP nanoparticles through calcium ion chelation, which helps protect them from endonuclease degradation [14]. Moreover HAp may penetrate cell walls and be consumed by cells, allowing for a high level of cellular absorption [15] and no harmful compounds released when HAp is broken down. Figure.1.5 shows the different stages of gene therapy using vectors.

Under physiological conditions, HAp has low solubility and can be used as a carrier for local drug delivery through surgical insertion or injection. HAp-based drug delivery systems include: i) drugs conjugated or loaded onto HAp scaffolds, ii) porous HAp granular nanoparticles, and iii) HAp nanoparticles coated with polymers. This controlled drug delivery with HAp reduces the drug concentration in the blood, minimizing toxicity by ensuring levels remain below the toxic threshold and above the effective base level. Due to its properties such as low cytotoxicity, large surface area, and ease of production and customization, HAp is a promising candidate for co-delivery systems that carry both genes and drugs into a single cancer cell [16].

### 1.7.3 Bone Void Fillers

A bone void is a cavity in the bone that arises due to the failure of the bone's self-healing mechanism. Such voids or damage in otherwise healthy bone tissue can be caused by infection, trauma, tumors, or complications following joint replacements. To address these voids or defects, bone grafts are used. The four main types of bone graft materials are autograft, allograft, xenograft, and alloplastic graft. Calcium-based materials are commonly utilized as bone grafts. Studies have shown that calcium hydroxyapatite (HAp) is an effective biocompatible and osteoconductive material that provides a scaffold for bone formation. The suitability of HAp as a bone graft replacement depends on its interconnectivity and pore size [17]. HAp has been used to promote alveolar bone regeneration, either alone or in combination with other graft types (auto/allo/xeno graft).

### 1.7.4 Desensitizing Agent in Post Teeth Bleaching

Tooth sensitivity, also referred to as "dentin hypersensitivity" (DH), is characterized by discomfort or sharp pain in the teeth triggered by specific stimuli, such as hot or cold temperatures. Gupta et al. explain that DH occurs when rapidly flowing fluid in the small tubules of dentine stimulates the nerve terminals at the pulp-dentine interface due to external stimuli, causing pain. Surveys indicate that DH affects between 74 to 80 percent of the adult population, depending on the region. An ideal treatment for DH would involve sealing the tiny holes or cracks in the tooth’s enamel with a professional desensitizer that either creates a barrier or fills in these small gaps. Recent clinical trials have shown that desensitizing agents based on nano-hydroxyapatite (n-HAp) are promising for treating DH.

### 1.7.5 Edentulous Ridge Augmentation

Ridge augmentation is a common dental procedure often performed following a tooth extraction. The alveolar ridge is the bone that supports the roots of the teeth in the jaw. After a tooth extraction, the alveolar ridge is left with an empty socket, and the bone's original width and height will gradually diminish (Figure.1.6 (a)). To place dental implants or for aesthetic reasons, it may be necessary to reconstruct the alveolar ridge to its original dimensions. This surgery aims to restore the natural contour of the jaw and gums (Figure.1.6 (b)).

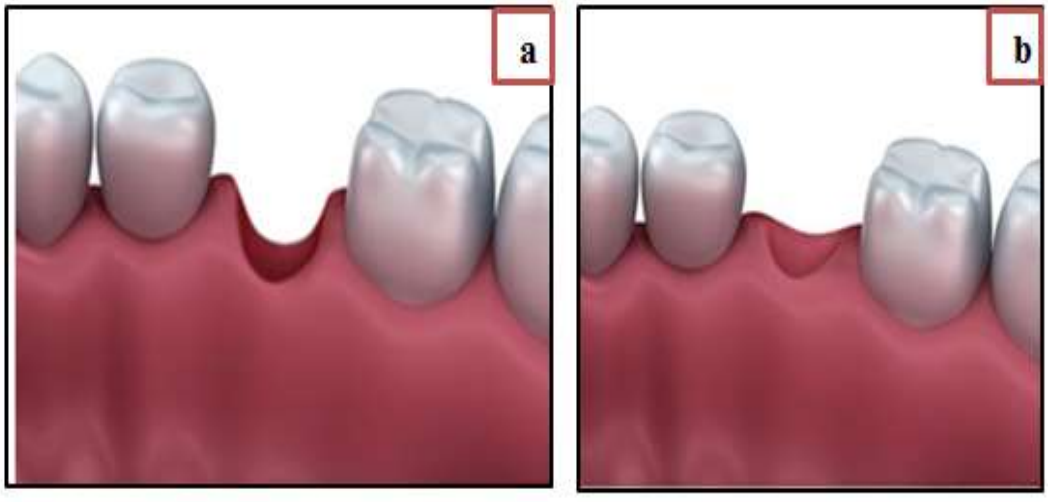


**Figure 1.6 Teeth (a) before ridge augmentation (b) after ridge augmentation**

Vertical bone augmentation can be achieved using gelatinous graft materials that contain HA nanoparticles. Research has demonstrated that high-viscosity gels offer greater bone augmentation. The

injection of nano-HAp gel is a minimally invasive technique with potential for effective bone augmentation [18].

### 1.7.6 Mending of Mechanical Furcation Perforations and Apical Blockade

Perforation involves creating an artificial connection between the root canal system and the supporting tissues of the teeth. Root perforations can occur pathologically due to resorption and caries, or iatrogenically following root canal therapy. This opening provides a route for bacteria to enter from the root canal or periodontal tissues, causing an inflammatory response that can lead to fistulas and bone resorption. When perforations occur laterally or in the furcation area, the gingival epithelium may grow towards the site, worsening the tooth's prognosis. Small perforations located apical to the crestal bone that are quickly repaired generally have a good prognosis. Hydroxyapatite can be used both as a direct repair material for perforations and as an internal matrix [19]. As a repair material, it helps restore bone lost due to iatrogenic root perforation. Additionally, when used as an internal matrix, it prevents the extrusion of dental filling materials such as glass ionomers and amalgam and serves as a permanent support structure for the repair material.

## 1.8 CONCLUSION

Nano-hydroxyapatite (nHAp) has garnered significant interest as a non-toxic biomaterial for prosthetic applications due to its excellent biocompatibility, bioactivity, slow degradation, and superior osteoconductivity. Its chemical similarity to the mineral components of hard tissues makes it suitable for use in artificial bones and tooth replacements. Substituting HAp with ions such as $Fe^{2+}$, $Mg^{2+}$, $Sr^{2+}$, and $Ag^{2+}$ can enhance the physicochemical, morphological, and mechanical properties of the resulting ceramic. This modification holds potential for developing new medical applications with improved bioactivity and osteointegration, while minimizing adverse complications.

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