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Materials used for bleaching and their effects on dental materials: a review

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Abstract: Over the years, bleaching agents were developed and new materials were introduced to facilitate the bleaching process for both the dentist and the patient. Several studies were made to evaluate the effect of such agents on different materials used in dentistry. This paper will describe different types of bleaching agents along with their possible effect on restorative materials.

Keywords: Bleaching**;** *Bleaching materials; Bleaching agents; Materials properties; Composite resin; Glass ionomer; Amalgam; bonding; Restorative materials.*

Tooth discoloration has been an ongoing problem affecting patients and making them seek treatment.Tooth discoloration can be intrinsic (affecting deeper layers of tooth structure), extrinsic (affecting outer tooth layer) or both. Causes of intrinsic tooth discoloration can be genetic conditions (amelogenesis imperfecta), systematic conditions (porphyria and jaundice), body byproducts (hemoglobin and bilirubin), trauma, restorative materials (amalgam restoration) and medications taken during tooth development (fluoride and tetracycline). Extrinsic tooth discoloration can be caused by chromogenic bacteria and plaque, tobacco and cigarettes, food and beverage, chemicals (chlorhexidine) and poor oral hygiene. Causes of both intrinsic and extrinsic discoloration can be either aging or fluorosis. Generally Extrinsic stains are easier to remove than intrinsic stains because intrinsic stains are stains that became incorporated inside tooth matrix. [1,4] Along the years, many advancements were made and many materials were discovered in order to solve this problem and get better results. the bleaching materials used will be discussed in this topic, along with the possible effects that bleaching materials may have on other materials used in dental field. [1, 2]

History of bleaching materials:

Non- vital tooth bleaching started as early as 1848 by using chloride of lime. Later, many materials were introduced as sodium hypochlorite solution and oxalic acid. In 1868, the first attempt to bleach vital tooth was made using oxalic acid and by 1911, hydrogen peroxide material was introduced with the possibility of using light or heating source along with it. In 1960, an orthodontist named Dr. Bill Klusmier introduced “over the counter” home bleach which contained 10% carbamide peroxide. Bleaching materials continued to develop. Nowadays,

there are home bleaching methods using lower concentrations and in office bleaching methods using higher concentrations. [3]

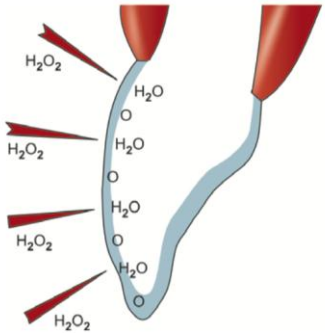
Composition of commercial bleaching materials:

1- Active ingredient:
Hydrogen peroxide, carbamide peroxide and sodium perborate.
2- Thickening agents
3- Surfactant
4- Carrier agent
5- Preservatives
6- Flavoring agents

1. Active ingredients:

1.1. Hydrogen peroxide: It is the most used material in bleaching agents. It is used in 5% to 35% concentrations.This range of concentrations is used according to method of use, stain severity and method of activation. Method of use affects concentration used as home bleaching uses low concentrations (5-10%) while in-office bleaching uses higher concentrations (30-35%); Stain severity affects the concentration used as lower concentrations are used for mild stains while high concentrations 30-35% are used for severe stains.[4] Method of activation affects the concentration of hydrogen peroxide used as new generation is introduced with low concentrations (3.5-15%) with semiconductor catalyst to potentate the oxidation reaction for in- office bleaching. This new generation is considered to be safer to use due to its lower concentrations.[14] Hydrogen peroxide was used in liquid form which is applied to the tooth, however it is now available in gel form. The gel form is preferred because it prolonged its shelf life and prevented its leakage from the tray. It is used in both in- office and home bleaching. [4]

Mechanism of action: Hydrogen peroxide divides into water and oxygen particles. Those unstable free radicals penetrates the tooth and remove the stain particles by attacking the double bonds. The break down of the double bonds results in smaller particles; This process affects the color absorption of the tooth and gives whiter appearance (fig.1) .[3]



Figure(1) The breakdown of hydrogen peroxide into water and oxygen particles that penetrates into the tooth structure causing oxidation of the pigments.

1.2. Carbamide peroxide: It is also known as urea hydrogen peroxide. It is used in concentrations from 3% to 45%. [4] Carbamide peroxide is available in gel form and can be supplied in syringe for ease of application since it can be used in home bleaching with low concentrations while high concentrations can be used in an in-office bleaching.

Mechanism of action: Carbamide peroxide breaks down to hydrogen peroxide and urea and thus is given the name urea hydrogen peroxide. The urea has many advantages which are stabilization of hydrogen peroxide and elevation of the PH (fig.2).[5]

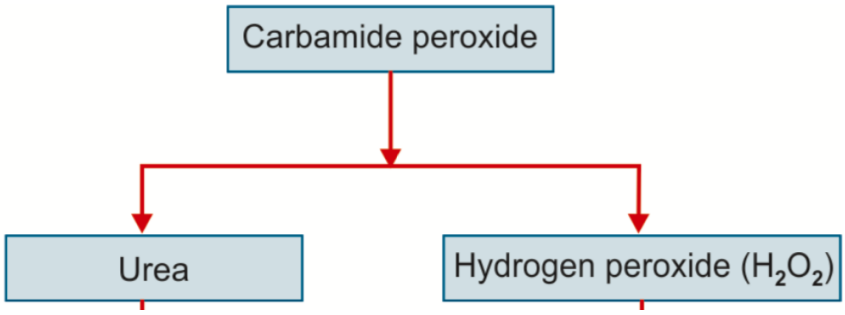


Figure (2) Carbamide peroxide mechanism of action by breaking down into urea and hydrogen peroxide.

1.3. Sodium perborate: sodium perborate powder is used with hydrogen peroxide due to their synergistic effect. Many recommended using such combination inside root canals in non- vital tooth bleaching.

Mechanism of action: Although sodium perborate does not contain hydrogen peroxide, it was found that when it breaks down, it releases hydrogen peroxide. Sodium perborate works more effectively with increasing the temperature over 55 ° c. To be able to be used in the temperature of the mouth, tetraacetylethylenedi- amine (TAED) organic activator is added to it. It should be noted that sodium perborate is banned in Europe and is considered as fetotoxic and cytotoxic material.[5]

2- Thickening agents: Carbopol (carboxypolymethylene) is the most used thickening agent used to increase the viscosity of the material and thus the material does not fall from tray. It also increases the time of oxygen release from the bleach material.

3- Surfactant: The surfactant is used to increase the efficacy of bleaching materials by increasing the wettability of the surface by them and so allow better diffusion of the materials inside the tooth.

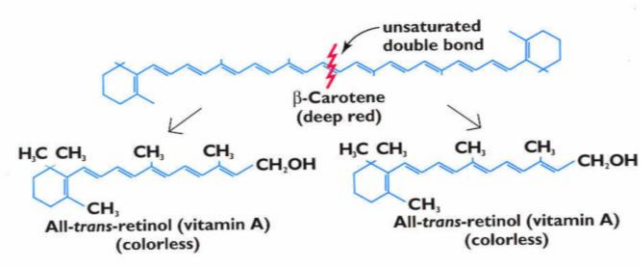
4- Carrier agent: Glycerin is used to help other ingredients to dissolve.

5- Preservatives: Sodium benzoate is used to prevent bacterial growth.

6- Flavoring agents: As peppermint, used to allow better patient acceptance. [3]

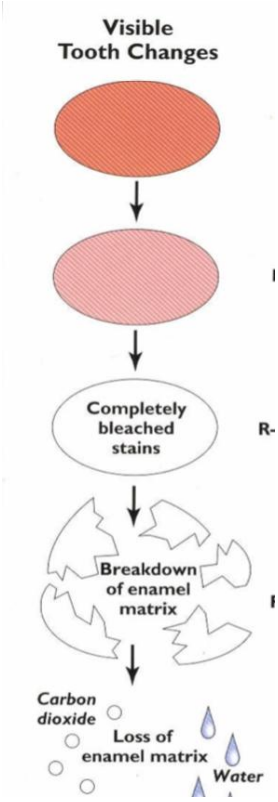
Pigment removal mechanism:

The process of pigment removal is through redox reaction, in which the hydrogen peroxide is oxidized forming free radicals. The free radicals released from the bleaching materials are unstable. They penetrate into organic matrix of the tooth structure and attack the bonds of the pigments to break the pigment into smaller structures that are colorless. An example can be beta carotene which is reduced by hydrogen peroxide free radicals into two colorless structures (fig.3).[6]



Figure(3) The reduction reaction of beta carotene into two smaller colorless structures

Saturation point: This occurs when all pigmented structures are changed into colorless ones. If bleaching material is left beyond this point, it will cause breakdown of the tooth structure which could lead to tooth brittleness and increase in porosity (fig.4).[6]



Figure(4) The saturation point is reached when all pigmented stains become colorless; Extended bleaching beyond this point will cause breakdown of the tooth matrix.

Techniques of bleaching:

Bleaching techniques can be classified into vital and non vital

For vital tooth:

- **Home bleaching:** Using 15% hydrogen peroxide or 1-10% hydrogen peroxide. A tray is made for the patient and the patient is instructed to put the material in the tray and wear the tray daily. Patient is called for checkups with the dentist to evaluate progress.

- **In-office bleaching**: There are 2 types, which are thermocatalytic and non thermocatalytic.

Thermocatalytic in-office bleaching is done using light source either conventional light or tungsten halogen light.

Apart from using heat to accelerate the radical release from hydrogen peroxide, there are methods that use light source in the presence of photosensitive agents or photocatalysts inside the bleaching materials that absorb the energy from the light/ laser and are activated to accelerate the hydrogen peroxide reaction(Photolytic reaction) and thus increase the amount of free radicals produced and the efficacy of bleaching material.[24]

Procedure: Teeth are isolated and polished. The bleaching material (30-35% hydrogen peroxide) is applied and the light is adjusted. Bleaching material is changed every 5 minutes and then finally removed.

Non-thermocatlytic in-office bleaching is done without the use of light source.

Procedure: teeth is isolated with rubber dam and then 30-35% hydrogen peroxide is applied for 5 minutes and then washed.[4]

- **Over the counter whitening products:**

As whitening kits, whitening tooth pastes, whitening chewing gum, whitening floss, whitening mouthwash,[5] whitening pens and whitening strips.Whitening pens release active oxygen that results in tooth whitening. Whitening strip is a flexible plastic that contains hydrogen peroxide or carbamide peroxide and is applied to the teeth by the patient; Since it is 2D strip, it can not be shaped according to the contours of teeth and so lacks precision. [25] Such materials may cause a lot of problems such as enamel erosion, loss of anatomy and tooth sensitivity because they are usually used by the patients without dentist supervision. The patient can overuse them or misdiagnose his condition.[5]

For non-vital tooth:

- **Thermocatalytic in-office bleach**

After tooth isolation, hydrogen peroxide and sodium perborate are used separately, or together and light source is applied.

- **Walking bleach (intracoronal bleach)**

Tooth is isolated and the coronal gutta percha of endodontically treated tooth is removed and then sodium perborate is applied inside the tooth. If the staining is severe 3% of hydrogen peroxide is used with sodium perborate. Temporary restoration is placed, and patient is recalled after 1-2 weeks. [4]

Factors affecting the bleaching agents efficacy:

1-Hydrogen peroxide concentration:

Using higher concentration of hydrogen peroxide leads to increase in its effect.

2- Temperature:
Every 10 ° c increase in temperature increases the rate of the bleaching chemical reaction by the double, however, the temperature increase should be within patient tolerance.

3- pH:
During storage, bleaching agents should be kept in acidic pH. The optimal pH for the reaction of the bleaching materials to take place is 9.5 to 10.8. In lower pH, bleaching materials tend to be less effective.[6] Due to its instability at alkaline pH, Hydrogen peroxide should be mixed with alkalizing solution just before use and therefore most of the bleaching materials comes in two syringes that require mixing.[15]

4- Time:
The effect of the bleaching materials is directly dependent on the amount of time it is exposed to the tooth.[6] Nevertheless, bleaching is done usually in three applications per one visit and the maximum time allowed is 15 -20 minutes per application. This may differ according to manufacture instructions.[16]

5- Method of activation:
Light activated bleaching materials result in increase in the free radicals produced by the bleaching material and so increase bleaching efficacy. [24]

Age restrictions of bleaching agents:
It was thought that bleaching is prohibited for children with deciduous teeth due to the large size of pulp chamber, however the american academy of pediatrics has approved the use of bleaching agents on both primary and mixed dentitions with lower concentrations of bleaching agents and under the supervision of a dentist.[18]

Contraindications of bleaching:
1- Emotional or psychological problems: loss of compliance.
2- Dentin hypersensitivity
3- Hypoplastic tooth: it will increase the color difference between the tooth structure and white spots.
4- Teeth with defective restorations.[4]
5- patients with photosensitive condition cannot undergo bleaching with light or laser. [25]
When Bleaching is contraindicated, several treatment options are available such as selective grinding of tooth (microabrasion), resin infiltration, composite restoration, veneers and full coverage crowns. [27]

Effect of bleaching materials on different dental materials properties:

1.Tooth structure:
Enamel: Erosion and loss of aprismatic layer was observed along with decrease in enamel surface hardness due to the degradation of enamel matrix by the bleaching materials. Decrease in calcium/ phosphorus ratio of enamel was also observed.

Dentin: Bleaching agents removed smear layer effectively from dentin, however, they left residue that affect the bonding of dentin with the adhesive and glass ionomer.[5] Bleaching agents and their thickening agents (carpabol) decreased surface hardness of dentin. [3]

Pulp: According to studies, bleaching materials can reach the pulp in 15 minutes and cause transient and reversible decrease in blood circulation to the pulp and glycerin present in bleaching materials can cause dehydration of tooth structure.[29] This can result in the patient feeling mild sensitivity after bleaching; This sensitivity increases with increasing the concentration of the bleaching agent used.[5]

Cementum: External root resorption and cervical resorption are reported to occur with non-vital tooth bleaching, but cementum is usually not affected by vital tooth bleaching.[5]

2.Composite resin:

Many studies were made on how the properties of composite resin restorative material were affected by the bleaching agents; Those studies had conflicting results, but they all agreed that some aspects of resin composite showed changes after bleaching.

Tensile strength: Microfilled composite resin showed decrease in tensile strength with bleaching while hybrid composite showed less significant change.This can be caused by the oxidative reactions of hydrogen peroxide that lead to degradation of polymer matrix and affect its cohesiveness and therefore composite resin having more concentration of resin matrix as in microfilled composite shows more degradation and decrease in tensile strength.[17]

Surface hardness: The effect of bleaching agents on surface hardness of composite resin is controversial. The depth of penetration of hydrogen peroxide is controlled by the concentration used and thus different concentrations of hydrogen peroxide have different impact on surface hardness.; For example, resin composite exposed to hydrogen peroxide with 14% concentration showed increase in hardness due to the fact that bleaching agent removed the surface layer and thus exposed more filler particles to the surface so the material showed increased surface hardness. On the other hand, resin composite exposed to 40% hydrogen peroxide showed decrease in surface hardness. This could be attributed to the release of the free radicals from bleaching agent causing debonding of filler and acceleration of the hydrolytic degradation.[7]

Bond strength

Torneck et al. (1991) discovered that the bond strength of freshly placed composite restoration made after bleaching is affected negatively by the bleaching materials. This could be attributed to the fact that newly bleached enamel has fewer, shorter and less defined resin tags in addition to the remaining oxygen on the surface of enamel causing inhibition of the polymerization to the resin composite.
It is therefore recommended to wait from 1 to 2 days up to 1 week following bleaching session before application of bond,[5] however, many recent studies suggested the use of ascorbic acid gel as antioxidant for 60 minutes after bleaching materials immediately showed improvement in bond strength. Although ascorbic acid can cause enamel erosion with prolonged exposure, the gel form of ascorbic acid slowed the rate of release of substance from the acid and thus allowed the use of ascorbic acid for longer times on tooth structure and increased its efficacy. (Kaya et al. 2008) .[19]

On the other hand, bond strength of an already existing composite restoration showed decrease after bleaching, which could be caused by the release of the free radicals which could attack the hybrid layer. The higher the concentration of the bleaching agent used, the higher the effect it has on the strength of the bond.[3]

Microleakage and bacterial adhesion: Increase in microleakage was observed in composite resin.[4] Microleakage should be differentiated from nanoleakage. Microleakage is the formation of gap between enamel/ dentin and restoration while nano leakage is nanoporosities formed within the hybrid layer even without marginal gap formation. [28]

Adhesion of salivary proteins was less after bleaching and this affects the adhesion of cariogenic bacteria to the tooth.[3]

Surface roughness and porosity: Composite resin showed increase in surface roughness and increase in surface porosities.[4] This is due to the softening of resin matrix and displacement of filler particles under the effect of the bleaching agent and the debonding of filler particles by the free radicals released (fig.5). [20]

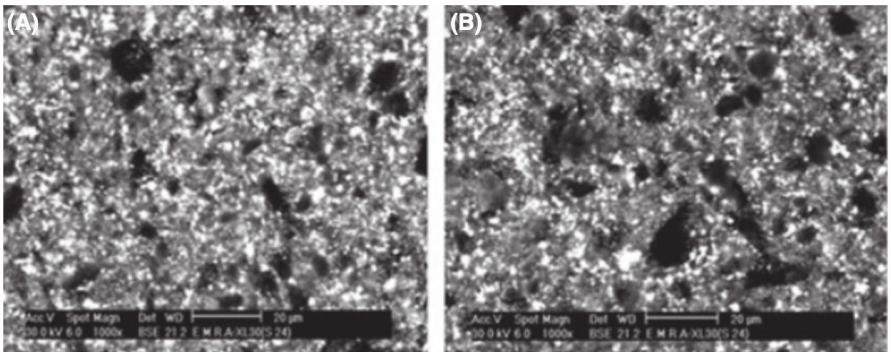


Figure (5) A) SEM of composite resin before bleaching. B) SEM of composite resin after bleaching showing increase in pores due to filler dislodgment.

Color stability: Color stability after bleaching was variable in different types of composite resin. This can be attributed to their different degrees of conversion and amount of fillers. The color stability of resin composite is dependent on the stability of its resin matrix. The color change of composite resin after bleaching is due to the oxidation of surface pigments. It is advisable to polish composite resin after bleaching to decrease the coloration that can be caused by the retention of microorganism to the rough surface caused by bleaching (fig.6).[3]

It should be noted that although these changes were detected, neither had real clinical impact.[5]

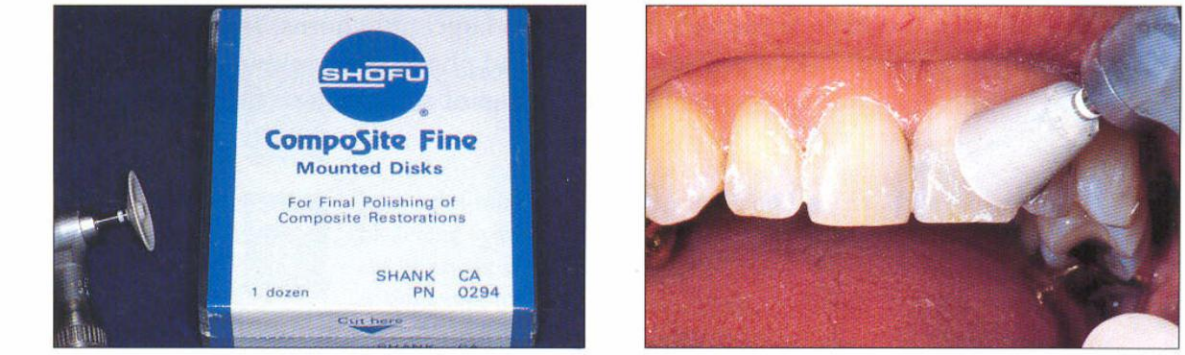


Figure (6) Polishing of composite resin following bleaching treatment is recommended to decrease the discoloration of composite restoration.

3. Amalgam restoration:

The effect of bleaching on amalgam restorations is mainly due to active oxidation process by the bleaching agents and microstructure changes within the amalgam.[8]

Surface hardness: No significant change in surface hardness of amalgam was detected after bleaching.[9]

Color stability:
Bleaching materials changed color of amalgam from black back to silver due to removal of the surface film of corrosion products formed [26]. Some amalgam showed greenish discoloration due to their copper composition.[5]

Corrosion:
Although studies made on the effect of the bleaching agents on amalgam restorations placed in the oral cavity suggested that bleaching agents caused increased release of mercury and other corrosive substances from the amalgam, they were found to be within the limit accepted by the world health organization.Unpolished amalgam showed more release of mercury compared to polished amalgam restoration, so it was recommenced to polish amalgam restorations and apply varnish before bleaching in order to limit the release of mercury.[10]

4. Dental alloys:
Corrosion: Bleaching agents have the same effect on dental alloys as on amalgam. They cause corrosion of the dental alloys, except noble alloys. It is also advisable to polish dental alloys before bleaching application to limit the release of the corrosive products.[8] A study made on different dental alloys showed that, except for gold alloys, all dental alloys (Ni–Cr–Mo, titanium) were liable to corrosion with bleaching agents. The rate of corrosion increased with increasing the concentration of bleaching agents used. The materials known for their passive layer were not able to maintain stable passive layer and the layer is usually destructed when exposed to bleaching agents due to high ion concentrations.[21]

5 Ceramics:
Surface hardness: Decrease in surface hardness was observed; this could be due to the decrease of SiO_2 that forms the matrix and thus affects the hardness.[22]
Color stability: Ceramics containing polymers showed color changes due to the polymer lacking chemical stability and thus is liable to color change when exposed to bleaching agents. Glazed porcelain showed no color change unlike unglazed porcelain.[11]

6. Provisional restoration:
Surface properties: Provisional materials showed cracking and swelling with hydrogen peroxide but appear to be unaffected by carbamide peroxide.[5]

Color stability: Methacrylate based provisional material showed orange discoloration with bleaching materials; On the other hand, bis- acryl composite based provisional materials showed no discoloration.[8]

7. Polymodified resin composite (compomer) and Glass ionomer cement:

Strength and hardness: Mechanical properties of glass ionomer such as compressive strength and hardness seem to decrease with bleaching agents;[12] This could be due to the alteration of glass iono-

mer matrix as it begins to erode when exposed to bleaching agents and the glass particles start to dislodge. Softening of glass ionomer occurs due to failure of bonds by the free radicals released from bleaching agents.[23]

Color stability: Color change with bleaching agents was also observed in compomers.[8] Glass ionomers shows the most noticeable color change of all esthetic restorative materials because it naturally lacks color stability due to the poly acid content and due to the degradation of its metal polyacrylate salts by the bleaching materials.[13]

Degradation and fluoride release: Bleaching agents with high concentrations used on compomers induced softening to the surface with surface degradation and increased fluoride release, however with smaller concentrations, there were no apparent changes in compomer nor glass ionomer.[8]

CONCLUSION

Bleaching materials, although advantageous for patients complaining from unappealing tooth discoloration, can cause many deleterious effects on other materials used in dentistry. Those changes can compromise their mechanical, physical or biological properties. Care and understanding of the chemistry of bleaching materials are necessary in order to prevent or decrease these effects to increase the durability of such materials and allow the patients to be satisfied with their teeth shade.

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Imperfections in solids

Myrna M. Elwaseef[1]

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Abstract: solids have strong attraction forces hold their particles together in proper arrangement. Throughout solids microstructure, perfect arrangement of atoms does not exist. There are always imperfections which influence the material properties. Imperfections have different classifications according to geometry or dimensionality of the defect.

Keywords: imperfections, vacancy, dislocation, burgers vector.

Introduction:

Perfect solids do not exist; all solids contain large numbers of various defects or imperfections. This applies to both crystalline and amorphous solids.

Crystalline imperfections in solids**:**

Any deviation from the perfect order arrangement of atoms, ions or molecules in crystal is called crystalline imperfection or defect.

Crystalline defect is defined as a lattice irregularity having one or more of its dimensions on the order of an atomic diameter.[1]

Classification of crystalline imperfections: according to geometry or dimensionality of the defect.

- Point defect (0 dimensional)
- Linear defect (one-dimensional)
- Plane defect (two-dimensional)
- Volume defect (three-dimensional)[1]

Point defects: are the irregularities or deviations from ideal arrangement around a point or an atom in a crystal. Those are associated with one or two atomic positions. Point defects may be created or modified by external ionizing irradiation, either by photons or by high-energy particles.

Types of point defects:

1- **Vacancy**: which is the simplest form of the point defects; it is a vacant atomic site in the structure fig.1. In fact, it is not possible to create such a material that is free of these defects. It is possible to eliminate all point defects except vacancies, as they arise from thermodynamics (entropy).[1] As the

temperature increases, the thermal vacancy concentration in pure metals dramatically increases, and makes an apparent contribution to different physical quantities of materials, such as heat capacity, melting point, diffusivity, thermal conductivity.[5]

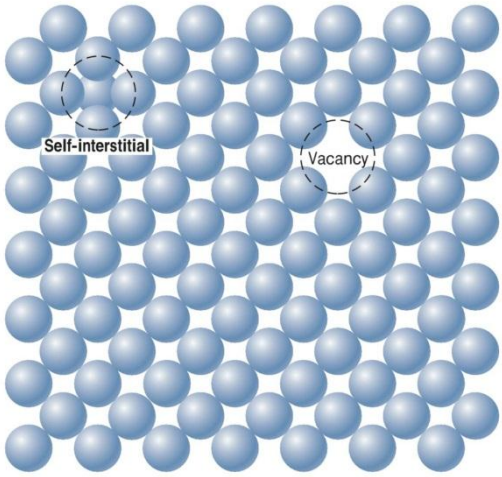

Fig.1 Two-dimensional representations of a vacancy and a self-interstitial.

The equilibrium number of vacancies (Nv) for a given quantity of material depends on the increase in temperature according to the following equation:

$$Nv = N \exp(-Qv/KT)$$

N is the total number of atomic sites, Qv is the energy required for the formation of a vacancy, T is the absolute temperature in kelvins, k is the gas or Boltzmann's constant=1.38 X 10^{-23} J/atom.

The number of vacancies is directly proportional to the temperature. For most metals, the fraction of vacancies Nv/N just below the melting temperature is 10^{-4}; that is, for each 10,000 atomic sites, there is only one site that is empty. [1]

2- **Self-interstitial:** is an extra atom from the crystal positioned between atomic sites (Fig.1). In metals, the atom is larger than the interstitial position in which it is situated, so there is a large distortion in the surrounding lattice. The equilibrium concentration of self-interstitials is very low compared to vacancies. [1]

3- **Impurities:** Metals cannot be obtained in a completely pure form; even with the most sophisticated manufacturing conditions, metals cannot be refined to purity greater than 99.9999%. Instead, they always contain small amount of impurities.[1]

There are two types of impurity point defects found in solid solutions: substitutional and interstitial.

a. Substitutional impurities: The impurity atoms replace the host or parent atoms (Fig.2). An example of a substitutional impurity is a copper atom preplacing or substituting a nickel atom from the nickel's lattice structure.
b. Interstitial impurities: Impurity atoms fill the voids or spaces between the host atoms (Fig.2). For metallic materials that have relatively high atomic packing factors, these interstitial positions are relatively small. In this case, the smaller atoms fit into interstitial spaces. Even very small impurity atoms

are larger than the interstitial sites, thus they introduce some lattice strains on the adjacent host atoms. [1]

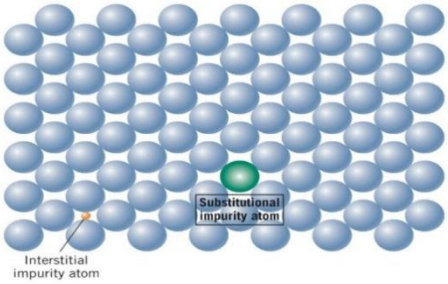

Fig.2 Two-dimensional schematic representations of substitutional and interstitial impurity atoms.

Point defects, whether interstitial atom, vacancy or impurity, cause space lattice distortion as shown in Fig. 3.

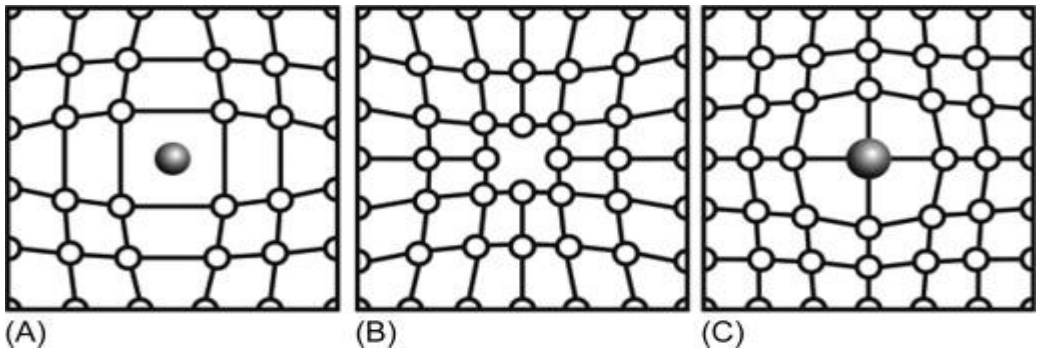

Fig.3. Schematic representation showing the space lattice distortion around interstitial atom (A), vacancy (B), and impurity atom (C)

Point defects in non-metallic crystals:

Point defects in non-metallic, particularly ionic, structures are associated with additional features (e.g. the requirement to maintain electrical neutrality and the possibility of both anion-defects and cation-defects existing).

- **Schottky defect:**
  It consists of a pair of an anion vacancy (an inion missing from the lattice site) and a cation vacancy (a cation missing from the lattice site). This maintains the charge neutrality (Fig.4.a)
- **Frenkel defect:**
  It consists of a pair of cations (positive ion) vacancy and a cation interstitial (Fig.4.b), or it may also be an anion (negative ion) vacancy and anion interstitial. However, anions are much larger than cations, so it is not easy for an anion interstitial to form.

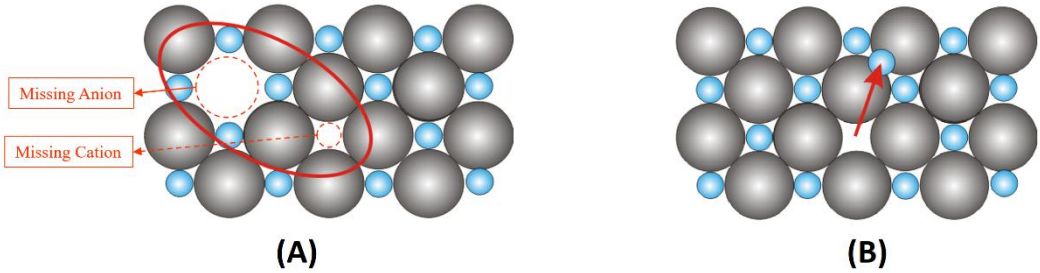

Fig.4. Schematic representation showing the Schottky defect (A) and Frenkel defect (B)

Linear defects / dislocations are defined as irregularities or deviations from ideal arrangement in entire row of lattice points, dislocation are a linear or one-dimensional defect around which some of the atoms are misaligned. [1]

There are three types of dislocations: edge dislocation, screw dislocation and mixed dislocation.

- **Edge dislocation/ dislocation line**: It is a linear defect that centers on the line that is defined along the end of the extra half-plane of atoms. At the region around the dislocation line, there is some localized lattice distortion which decreases as the distance from the dislocation line increases. Above the dislocation line in Fig.5 the atoms are squeezed together, and below the line, they are pulled apart; this results in a slight curvature in the vertical planes of atoms. [1]

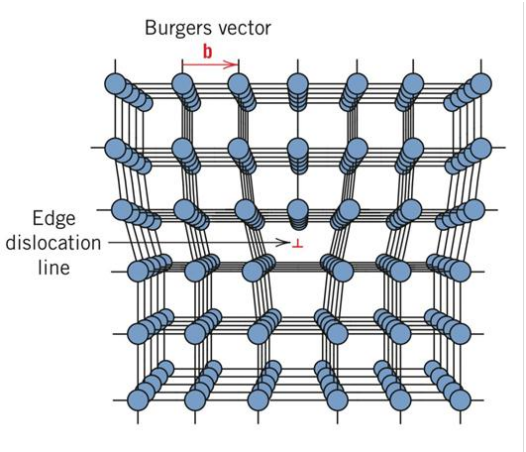

Fig.5. the atom positions around an edge dislocation; extra half-plane of atoms shown in perspective

Screw dislocation: Another type of dislocation may be thought of as being formed by a shear stress that is induced to produce the distortion shown in (Fig.6). The upper front region of the crystal is shifted one atomic distance to the right relative to the bottom portion. [1]

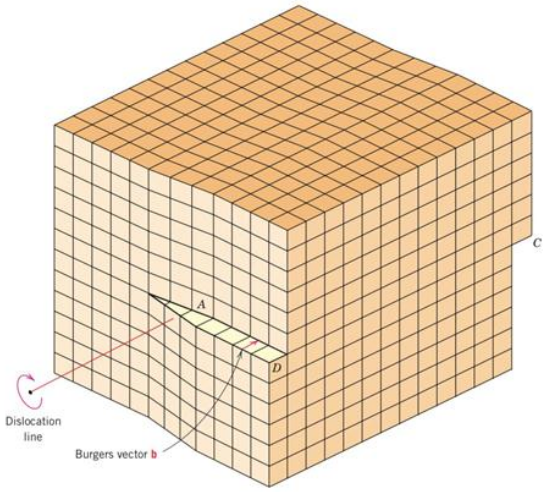

Fig.6 Screw dislocation within a crystal.

The atomic distortion associated with a screw dislocation is also linear and along a dislocation line. The screw dislocation derives its name from the spiral path that takes around the dislocation line. The motion of a screw dislocation that results from the induced shear stress is shown in (Fig.7). For a screw dislocation, lattice strains are pure shear only.[1]

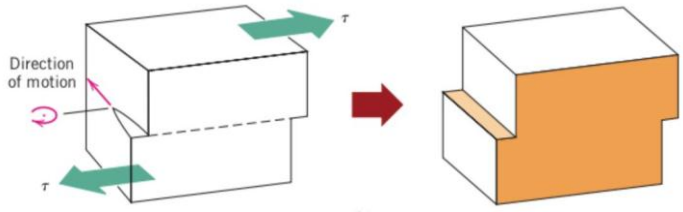

Fig.7. Formation of a step on the surface of a crystal by the motion of a screw dislocation

Comparison between edge dislocation and screw dislocation:[8]

Table.1. Comparison between edge dislocation and screw dislocation.

	Edge dislocation	Screw dislocation
Definition.	1-D line defect that is the edge of an extra half plane of atoms within the crystal lattice.	1-D line defect in which a path spirals around a dislocation line through individual parallel planes.
stresses	Tensile, compressive and shear stress fields my be present.	Only shear stress field exist.
Lattice disturbance	Region of lattice disturbance extends along an dislocation line.	Lattice disturbance extends in two separate planes at right angle to each others.
Burger's vector	Burger's vector is always **perpendicular** to the dislocation line.	Burger's vector is always **parallel** to the dislocation line.
Formation	Formed during formation and crystallization.	Formed during formation and crystallization.

Mixed dislocation: Most dislocations found in crystalline materials probably exhibit components of both edge and screw dislocation types; these known as mixed dislocations. All three dislocation types are represented schematically in (Fig.8); the lattice distortion that is produced away from the two faces is mixed, having varying degrees of screw and edge character.[1]

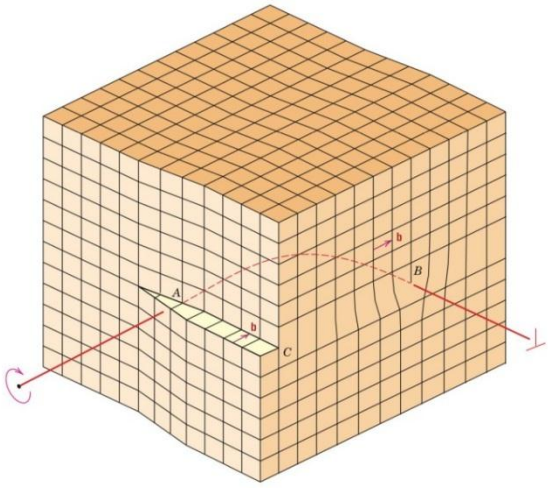

Fig.8. Schematic representation of a dislocation that has edge, screw, and mixed character.

Influence of point and plane defects on the material's properties and behavior:

1. Role of point defects in atomic diffusion
2. Effect of vacancies on thermal conductivity
3. Role of dislocations in plastic deformation of metals
4. Effect of dislocations and point defects on the electrical properties
5. Effect of dislocations and point defects on the optical properties

1. Role of point defects in atomic diffusion:

Point defects play an important role in atomic diffusion. Atomic diffusion can occur by two different mechanisms:

a) Vacancy Diffusion: It involves the interchange of an atom from a normal lattice position to an adjacent vacancy, as shown in (Fig.9). Of course, this process demands the presence of vacancies, and the extent to which vacancy diffusion can occur depends on the number of these defects are present.[1]

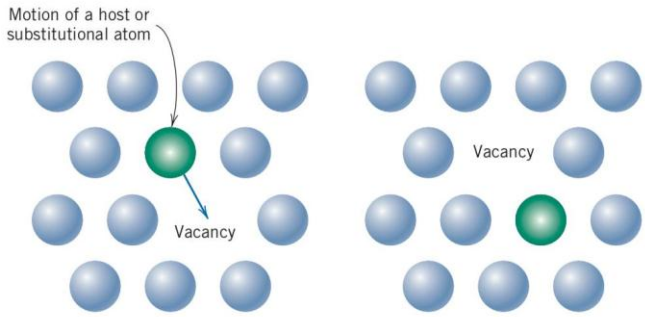

Fig.9. Schematic representation of vacancy diffusion

b) Interstitial Diffusion: The second type of diffusion involves atoms that migrate from an interstitial position to a neighboring one that is empty. This mechanism is found for inter-diffusion of impurities such as hydrogen, carbon, nitrogen, and oxygen, which have atoms that are small enough to fit into the interstitial positions (Fig.10). In most metal alloys, interstitial diffusion occurs much more rapidly than diffusion by the vacancy mode, because the interstitial atoms are smaller and thus more mobile. Furthermore, there are more empty interstitial positions than vacancies.[1]

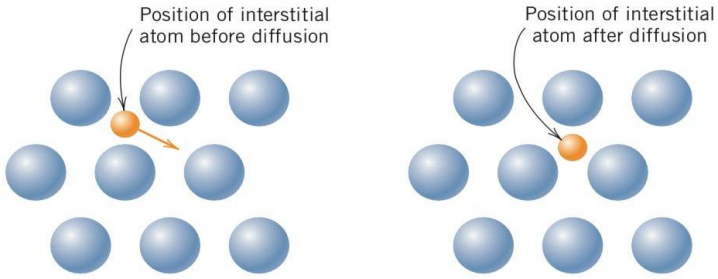

Fig.10. schematic representation of interstitial diffusion.

2. Effect of vacancies on thermal conductivity:

It was found that the thermal conductivity of the crystalline material decreases with the increase in the vacancy concentration. The presence of vacancies in the lattice structure elongates the “heat flux path” that the energy carriers follow during heat conduction.

3. Role of dislocations in plastic deformation of metals:

Dislocations are most significant in metals and alloys since they provide a mechanism for plastic deformation. Plastic deformation refers to irreversible change in shape that occurs when the force or stress that caused it is removed. In elastic deformation, the shape change is only a result of stretching of interatomic or interionic bonds, while in plastic deformation, the interatomic bonds are broken and new bonds are formed.[6]

A slip is the process by which plastic deformation is produced by dislocation motion. Slip between crystal planes result when dislocation moves, producing a permanent plastic deformation.

The vector representing the magnitude of the local slip, or more generally the difference in the amounts of local slip in neighboring regions, is known as the Burgers vector.[3]

An edge dislocation moves in response to a shear stress (Fig.11). Let the initial extra half-plane of atoms be plane A. When the shear stress is induced as shown in (Fig.11.a), plane A is pushed to

the right; this in turn pushes the top halves of planes B, C, D, and so on, in the same direction (Fig.11.b). The extra half-plane, moves from left to right by successive and repeated breaking of bonds and shifting by interatomic distances of upper half-planes. Before and after the movement of a dislocation through some particular region of the crystal, the atomic arrangement is ordered and perfect; it is only during the passage of the extra half-plane that the lattice structure is disrupted. This extra half-plane may appear from the right surface of the crystal, forming an edge that is one atomic distance wide; this is shown in Fig. 11.c.[1].

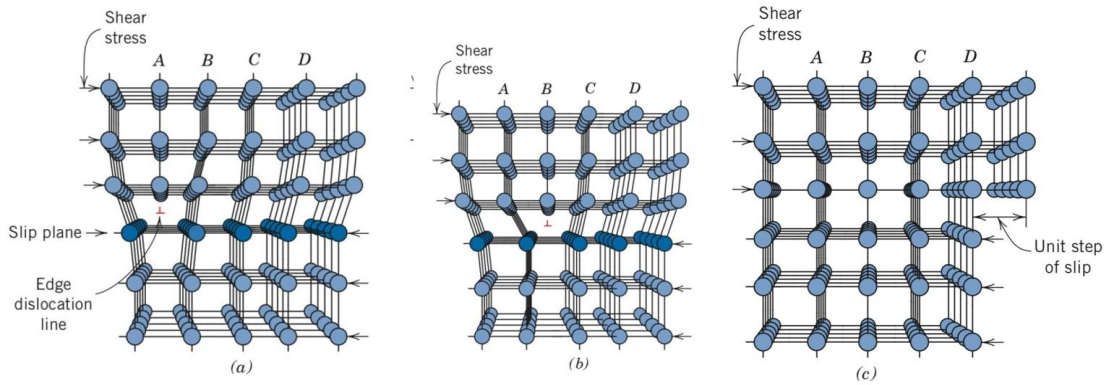

Fig.11. Atomic rearrangements that accompany the motion of an edge dislocation as it moves in response to an applied shear stress. (a) The extra half-plane of atoms is labeled A. (b) The dislocation moves one atomic distance to the right as A links up to the lower portion of plane B; in the process, the upper portion of B becomes the extra half-plane. (c)A step forms on the surface of the crystal as the extra half-plane exits.

It is noteworthy that in absence of dislocations (which is a hypothetical assumption), producing a permanent deformation in the metal would require breakage of bonds along an entire atomic plane. This would need an enormous amount of energy. On the other hand, in the presence of dislocations, the permanent deformation occurs by breakage of bonds along one row of atoms at a time, making the deformation much easier.

An often quoted analogy to show the effect of dislocations on facilitating slip movement is that of moving a carpet. Dragging the carpet across the floor is difficult because of the friction developed from the contact of the surface of the carpet with the floor. Imagine what would happen, however, if a wrinkle is put into the carpet, as shown in Fig.12. The carpet can now be moved by pushing the wrinkle across the floor, because only the friction between a small section of carpet and the floor has to be overcome. A similar phenomenon occurs when one plane of atoms moves past another by means of a dislocation defect. [6]

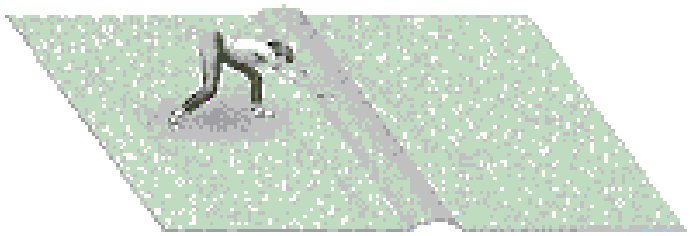

Fig.12. An analogy on how dislocation facilitates slip movement in metals

These dislocation-facilitated slip movements explain why the actual measured strength of metals is much lower than the predicted theoretical value calculated from the strength of the metallic bond (It was shown that the actual strength of metals is 10^3 to 10^4 times lower than their theoretical strength).[6]

Based on the previous discussion, it is clear that the slip provides ductility in metals. For example, if no dislocations were present, an iron bar would be brittle and could not be shaped by metal working processes. Material scientists actually make use of this fact when it comes to strengthening of metals. The mechanical properties of a metal or alloy can be increased by interfering with the movement of dislocations. An obstacle introduced into the crystal prevents a dislocation from slipping unless we apply higher forces. Thus, any mechanism that impedes dislocation motion makes a metal stronger.[6]

During the plastic deformation process, many dislocations move along the same slip plane until they encounter a barrier, such as a grain boundary, which prevents them from moving further. Thus, the dislocations pile up behind this barrier as shown in Fig.13. The interaction between these dislocations creates a back stress that makes it more difficult for further dislocation movements to occur. This explains the work hardening that metals experience during cold working.[7]

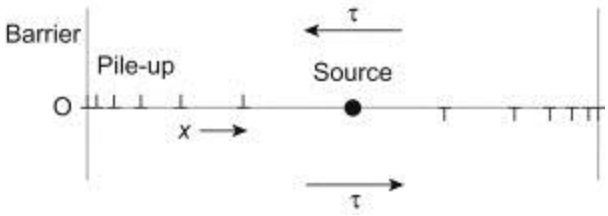

Fig.13 Linear arrays of edge dislocations piled-up against barriers under an induced shear stress τ

4. Effect of dislocations and point defects on the electrical properties:

Dislocations and other defects (including point defects) also influence the electrical properties of materials by interfering with the motion of charge carriers. This is why we make sure that the dislocation densities in single crystal silicon and other materials used in electrical applications are very small. Point defects also cause increased resistivity in metals.[6]

5. Effect of dislocations and point defects on the optical properties:

Both dislocations and some point defects act as light scattering centers within the material leading to an increase in its opacity. That is why the dislocation density affects the performance of photo detectors, light emitting diodes, lasers, and solar cells.

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Bone Cements

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Abstract: The demand for bone substitute materials have grown significantly in the last decade. The increasing size of the elderly population and the number of road traffic accidents could be attributed to this rapid rise. Accidents and trauma may result in bone defects that exceed a critical size, where surgical management is still considered a significant challenge worldwide.

Keywords: Bone cements, bone defect, calcium phosphates,

Introduction:

The demand for bone substitute materials have grown significantly in the last decade. The increasing size of the elderly population and the number of road traffic accidents could be attributed to this rapid rise. Accidents and trauma may result in bone defects that exceed a critical size, where surgical management is still considered a significant challenge worldwide.

When a defect heals only in the presence of bone graft material, it is considered critical-sized defect. A critical-sized defect is defined as the smallest size of a bone wound that does not heal spontaneously during the animal's lifetime. For example, critical-sized defects in a rat calvaria, mandible, and long bone are 8, 4, and 12 mm, respectively. At the same time, those in a rabbit are 15, 5, and 6 mm. In this type of defect, spontaneous healing does not lead to complete bony defect closure. While, on the other hand, formation of connective tissues is faster than the formation of new bone. Therefore, restoring such defects requires an intervening surgical procedure that usually involves bone substitute material. (1, 2)

Terminologies:

Bone graft: is defined as a living tissue capable of promoting bone healing, transplanted into a bony defect, either alone or in combination with other materials.

Bone substitute: is a natural or synthetic material, often containing only a mineralized bone matrix with no viable cells, that can promote healing.

Bone cements: are family of materials that consist of a powder phase and a liquid phase which after mixing form a plastic paste which can self-set once implanted in the body.

Uses of bone cements:

To fill a bony defect.

Mixed with autograft to compensate for its limited availability.

The fixation of screws in mechanically poor bone.

Bone augmentation.

Drug carrier.

Scaffolds.

Ideal properties of a bone cement:(3, 4)

An ideal bone replacement material elicits no adverse reactions following its implantation. It integrates with the host bone to induce the formation of new bone tissue, while being completely resorbed in the process.

Four fundamental biological properties are paramount in performing this role effectively; osseointegration, osteogenesis, osteoconduction, and osteoinduction.

Osseointegration is the ability of a grafting material to chemically bond to the surface of the bone in the absence of an intervening fibrous tissue layer.

Osteogenesis is the formation of new bone via osteoblasts or progenitor cells present within the grafting material.

Osteoconduction is to the ability of a bone grafting material to generate a bioactive scaffold on which host cells can grow.

Osteoinduction is the recruitment of host stem cells into the grafting site, where local proteins and other factors induce the differentiation of stem cells into osteoblasts.

Ease of handling

In vivo setting and hardening with appropriate setting times

Low setting temperature

Near neutral pH during setting

No disintegration in early contact with body fluids

No shrinkage during setting

Appropriate mechanical strength

High radiopacity

No toxicity

Biocompatibility

Bioactivity

Porosity.

- **Classification of bone substitute materials:**

The general classification divides all bone substitute materials into autografts, allografts, xenografts, and alloplasts. **Autografts** are bone grafts obtained from the patients themselves, whereas **allografts** are obtained from donors of the same species. **Xenografts** are bone substitutes derived from animal sources. The remaining nonbiological materials, such as ceramics, metals, alloys, polymers, composites, and hydrogels are listed under **alloplasts** and synthetic materials.

Acrylic bone cements (ABCs):

The term "bone cement" was initially applied to ABCs since the 1960s. ABCs are polymeric materials (polymethyl methacrylate), which cure through a polymerization reaction and produce a stable, nonresorbable material. (3)

Acrylic bone cements are mainly used to achieve mechanical stability by distribution loads evenly and transferring it to bone. ABCs are used for primary fixation of metallic component and for even load distribution.(3)

ABCs have some drawbacks:

- In some cases aseptic **loosening** occurs with time leading to mechanical failure of the cement.
- **Heat** released during the setting stage can induce bone necrosis (50-90°C).
- Wear particles and debris of the bone cement can cause **foreign body reaction** inducing osteolysis.
- **Monomer toxicity**.
- **Non resorbable.**
- **Polymerization shrinkage** of the acrylic cement.

Modifications of the formulation of ABCs are being investigated, aiming to improve their biological properties as: (3)

- The substitution of initiators, accelerators or radiopacifying agents by more biocompatible compounds,
- The addition of other monomers to the liquid phase that improve the biological performance of ABCs.

Bone Minerals' content:

The mineral phase of bone has an apatite crystalline structure which can exist in a range of compositions. So called **non-stoichiometric** or **calcium deficient hydroxyapatite (CDHA).** For stoichiometric hydroxyapatite with molar Ca/P ratio is 1.67 and for CDHA the molar Ca/P ratio is nearly 1.50. In fact, biological apatite is a carbonate containing CDHA, which in addition, contains several other ionic substitutions such as Na^+, K^+, Mg^{2+}, F^- and Cl^-. (3)

Calcium Phosphate Cements (CPCs):

CPCs were discovered by Legeros and (Brown and Chow) in the early 1980s [5]. This was an important break through as it supplied a **moldable material** which can adapt to the shape of the bone cavity, presenting a **good fixation** and providing **optimum tissue–biomaterial** contact to stimulate the bone ingrowth, thus providing osteo-integration and osteo-conduction. Moreover, CPCs are **resorbable,** with a resorption rate that depends on their composition and microstructural features. The properties mentioned give CPCs high bone regeneration potential. On the other hand, they have some limitations related to their **poor mechanical properties**. Thus used in non-load bearing application as cavity filling and enhancement of bone regeneration. [3]

CPCs are formed by a combination of one or more calcium phosphates, which upon mixing with a liquid phase (water or an aqueous solution) form a paste which is able to set and harden after being implanted within the body. The cement sets as a result of a **dissolution and precipitation** process. The entanglement of the precipitated crystals is responsible for cement hardening. [3]

Classification of calcium phosphates:

- **According to the end product (Hydroxyapatite, brushite & monetite in few cases).**

Hydroxyapatite is precipitated when the pH value of the paste is **above 4.2.** Apatite cements have higher mechanical strength than brushite. Yet, it has slow rate of resorption in vivo that interferes with the bone regeneration process.

Some CPCs have been designed to form **brushite** as the end product. Brushite is an acidic calcium orthophosphate, which is metastable under physiological conditions. For this reason, brushite CPCs are much more quickly resorbable than apatite CPCs and may convert into HA. All brushite CPCs are obtained because of an acid–base reaction. The paste of brushite CPCs is acidic during setting because brushite can only precipitate at a pH **lower than 4.2**. After setting, the pH of the cement paste slowly changes toward the equilibrium pH. The setting reaction is more exothermic than apatite forming cements. [3]

- **According to the setting reaction (Acid-base reaction & hydrolysis).**

CPCs can also be formed by two reactants, one of them an acidic calcium orthophosphate and the other a basic calcium orthophosphate, which set following an **acid– base reaction**. The most widely studied combinations are tetra-calcium phosphate TTCP (basic) + dicalcium phosphate dihydrate DCPD (acidic) and TTCP (basic) + dicalcium phosphate DCP(acidic) mixtures that form HA or CDHA.

In **hydrolysis** of a metastable calcium orthophosphate in aqueous media, CPCs are formed of only one calcium orthophosphate. The solid part of such formulation is called single phase cement powder. Thus, the cement is made of one type of calcium phosphate (ACP) and aqueous solution. (3)

- **According to the temperature at which precipitation occurs (CP obtained at high temp, & CP obtained at ambient temperature)**.

Setting time:

The setting time of a CPC can be defined as the time required for the initial setting of the cement paste, which is reflected in loss of plasticity.

Ideally, the initial setting time should allow sufficient time for shaping and filling. After filling, the set cement should not be disturbed till hardening occur as any mechanical strain during this period can adversely affect the strength.

The proposed ranges for the initial and final setting time were $\mathbf{4 < \mathit{I} < 8\ min}$ for the initial setting time and $\mathbf{10 < \mathit{F} < 15\ min}$ for the final setting time. Thus, providing enough time for filling and shaping of the cement in the bony defect. Then hardening of the cement occurs. (6)

Setting times of **apatite CPCs** are too long and several strategies can be applied to reach the clinical requirements as:

- The liquid-to-powder ratio (a smaller amount of liquid reduces the setting time),
- The reduction of the powder size (smaller size shorter setting time),
- The addition of calcium or orthophosphate ions either predissolved in the liquid phase or as highly soluble salt (common ion effect: the higher the concentration, the shorter the setting time),
- The addition of seed materials, which act as crystal nuclei (the more the nuclei, the shorter the setting time).

On the other hand, brushite CPCs tend to set too quickly. The setting time of brushite CPCs is controlled by the solubility of the basic phase: the higher the solubility, the faster the setting time. In brushite CPCs, setting retarders are often used as an approach to increase the setting time. (3)

Microstructure and porosity

The setting reaction of a CPC consists of the dissolution of one or more constituents of the cement powder and the precipitation of a different calcium orthophosphate. Physically, it takes place by the entanglement of the crystals of the precipitating calcium orthophosphate.

In cements that set by acid base reaction, liquid is required only to make the reactants workable and to allow homogeneous reaction. In other cases, when a hydration reaction takes place, some water is consumed, but much less than the total amount added to make a workable paste.

Water is a major contributor to the origin of porosity in this system and therefore CPCs are intrinsically porous materials. The porosity of the set CPC is closely related to the **liquid-to-powder ratio** used and it normally varies between 30% and 50%. although even higher values can be reached. The pores are normally micro- or nanometric in size and **the particle size** of the starting powder can modify the size of the precipitated crystals and also the pore size distribution. [3]

Porosity is an important factor for the cement degradability. It allows proliferation, migration, and invasion of cells into the cement. Moreover, it provides space for the newly formed bone to grow in.

Several different aspects of the porosity are important for the osteoconductive properties:

- Pore size
- Total porous volume, (the relationship between pore volume and specimen volume)
- Interconnectivity of the pores.

Pore size can be divided in two different groups:

- **Microporous** (<5-μm pores)
  Important for the bioresorbability of the material.
- **Macroporous** (>100-μm pores).
  Large macroporosity (i.e., 400–600 μm) facilitates infiltration by fibrovascular tissue and revascularization, allowing bone reconstruction. The optimal macroporosity for the ingrowth of bone tissue ranges between 150 and 500 μm. [7]

Total pore volume

Porous materials have the advantage of allowing circulation of body fluids and increasing the potential for firm attachment of body tissue. However, the disadvantage of a larger total porous volume is a decrease in mechanical strength. For example, an increase of the total porous volume from 10 to 20% results in a decrease in mechanical strength four folds. [7]

Interconnectivity

The pores may either be interconnecting or they con- tain “dead-ends.”

Biomaterials with interconnective pores are superior to biomaterials containing dead-end pores because a spatial continuous connection of the pore system allow the ingrowth of new bone. [7]

Strength of CPCs:

Since these materials are used as bone substitutes, it is important to keep in mind the reference values of the compressive strength of human cortical bone that ranges between 90 and 209 MPa and that of the cancellous bone between 1.5 and 45 MPa.

Factors that affect the strength of the CPC:

- The chemical composition
- The liquid-to-powder ratio
- The particle size of the reactants
- The crystallinity
- The use of liquid accelerators

Different studies reported that the compressive strength of apatite cements normally ranges between 20 and 50 MPa. Brushite CPCs are in general weaker than apatite CPCs and compressive strengths of 25 MPa have been reported. . [3]

Solubility

- Calcium phosphate ceramics can dissolve in basic, neutral, or acid solutions depending on their chemical composition.
- In **acidic environments** calcium phosphate ceramics dissolve **rapidly**.
- Ca/P ratio of the CPC is important for the dissolution process. TCP (Ca/P <1.67) dissolves 12.3 times faster than HA (Ca/P = 1.7). [7]
- Other properties of the biomaterial influence its solubility:
  - ⇒ Porosity
  - ⇒ Crystallinity
  - ⟹ Presence of impurities

Biocompatibility

Biocompatibility can be defined as the ability of a material to perform with an appropriate response in a specific application.

Three different levels of biocompatibility can be distinguished: inert, bioactive, or biodegradable

- **Bioinertness**

Bioinertness means that no chemical interaction takes place between the implant material and host tissue.

- **Bioactivity**

Bioactivity can be described as the occurrence of an interaction between a biomaterial and the surrounding tissue.

The interaction consists mainly of the formation of a layer of hydroxyapatite on the surface, whereas the bulk of the material remains unchanged. This layer of hydroxyapatite increases integration

- **Bioresorption**

Bioresorption is a biological mechanism by which certain ceramic materials resorb partially or completely and thereby disappear partially or completely over a period of time. Ideally, the rate of resorption is similar to the rate of formation of new bone. . [7]

In vivo resorption and remodeling

⇒ CPCs are highly biocompatible osteoconductive materials and can stimulate tissue regeneration.

⇒ Brushite CPCs are resorbed in vivo much faster than apatitic cements because brushite is metastable in physiological conditions. However, it has been reported that brushite CPCs tend to transform to HA in vivo, this transformation reducing its overall degradation rate. The addition of magnesium salts can be used to avoid or at least delay this transformation.

Factors affecting the degradation rate of CPCs:

- Chemical composition
- Crystallinity of the final product
- Porosity of the set cement

To accelerate the resorption of apatite CPCs incorporation of **macroporosity** is done, which is a method used to facilitate bone ingrowth, not only from the external surface, but throughout the whole bulk of the material. This would accelerate its resorption and its transformation in newly formed bone tissue.

Two different strategies have been adopted to introduce macroporosity in CPCs:

- The first approach: aims to produce the macropores **after the cement set**. by adding different porogenic agents such as sugars, PLA fibers or particles to the CPC paste. After setting, the porogenic agents degrade faster than the cement itself, creating the macroporosity.

Disadvantage: It is necessary to add a large amount of porogenic agent to guarantee interconnectivity of the macroporosity, thus compromising the excellent bioactivity and biocompatibility of CPCs.

- The second approach: cement paste is foamed **while it has a viscous consistency** and its setting creates a solid macroporous construct. This could be done by the addition of some gas-generating compounds, such as hydrogen peroxide.

Disadvantage: the liberation of gas after the implantation of the cement paste could have harmful effects on the organism. (3)

Modifications in CPCs

HA-based bone substitute materials:

Producing nano-sized HA, which showed enhanced biomechanical properties and mimicing the composition of natural bone. (4)

The rationale for development of these nanosized materials include:

- Much closer resemblance to bone extracellular matrix.
- Nanocrystalline HA exhibits improved biological performance and dissolution compared with its conventional forms of HA.
- Enhanced delivery and controlled release of bioactive molecules, such as growth factors, allowing for
  nced osteo-regenerative properties.
  nanostructure allows for a larger surface to volume ratio, promoting more effective adhesion, proliferation, and differentiation of osteogenic progenitor cells , enhancing new bone formation, resulting in improved fracture toughness and other mechanical properties. (4)

Biphasic Calcium Phosphate Ceramics (HA and β-TCP Ceramics)

- This combination resulted in more rapid and higher bone regeneration rates seen compared with the use of HA alone and the greater mechanical properties than β-TCP alone. Additionally, the resorption and osteoconductivity of biphasic calcium phosphate ceramics can be controlled by altering the ratio of HA/β-TCP.
- Despite the improvements in mechanical strength compared with β-TCP alone, biphasic CP ceramics still possess compressive strengths lower than that of cortical bone. The use of biphasic CP ceramics has been indicated as a bone substitute in periapical surgery and showed complete alveolar bone healing over a two year period. (4)

Combination with osteogenic substances

Bioactive molecules such as bone morphogenetic proteins (BMPs) play an important role in the process of differentiation.

Despite the osteogenic capacity of bone marrow, it cannot be used as a spatial filler.

Therefore, when used in combination with bone replacement materials such as calcium phosphates the later can supply the matrix, osteoconductivity, and a bioactive surface for the osteogenic bone marrow. [7]

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Effect of erosive conditions on tooth-colored restorative materials

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Abstract: Dental erosions are defined as "loss of dental hard tissue due to repeated acid attacks in the absence of the biofilm plaque and without the involvement of bacteria" [1]. Since the etiology shows multiple reasons for the hard tissue loss, the term biocorrosion was recently introduced in the dental literature [2]. This term includes endogenous and exogenous acidic impacts, as well as proteolytic degradation of the teeth induced by proteases, such as pepsin, from the gastric fluid which can destabilize the collagen network of the dentin. We will discuss the effect of erosive conditions on tooth colored restorative materials.

Keywords: *Dental erosion, composite, glass ionomer, ceramics*

Etiology of dental erosion

The acids responsible for the demineralization and loss of hard tissue substance might be from endogenous origin as stomach acid, gastroesophageal reflux disease (GERD) and eating disorders as bulimia or anorexia or from exogenous sources from dietary compounds like acidic beverages or food, citrus juices, and soft drinks [3].
N.B: Aggressive dental erosion is seen in patients with low salivary flow, xerostomia or low salivary buffering capacity because Saliva is considered an important biomodulating factor in dental erosion. It can clear and neutralize erosive acids, form acquired dental pellicle and remineralizes eroded tooth structure [4], figure (1).

Figure 1. Cases of the loss of dental hard tissue (erosion).

Consequences of erosion

Repeated exposure of the tooth enamel to acids results in dissolution of hydroxyapatite and softening the enamel surface making it susceptible to further mechanical abrasion. Therefore, the term erosive tooth wear was created for this two-step chemical–mechanical process [5].

Two actions are responsible for the erosively induced tooth wear observed in the oral cavity:

1. The dissolution and loss of dental hard tissue, which is directly induced by the acid attack.
2. The wear of the softened surface by mechanical impacts, such as toothbrushing, rubbing with the tongue, tooth-to-tooth contacts or chewing of food.

A recent study has shown that tooth erosion with low severity did does not impact oral health-related quality of life in 11- to 14-year-old children. In contrast, adult patients with non-cariogenic dental hard tissue loss have shown up with [1,5]

1. Reduced oral health and compromised esthetic appearance of the teeth.
2. Reduced chewing efficiency.
3. Tooth pain and hypersensitivity due to the exposed dentin areas.

In severe situations, as in GERD, a significant loss of tooth structure leads to loss of vertical dimension and function and pulp exposure [5].

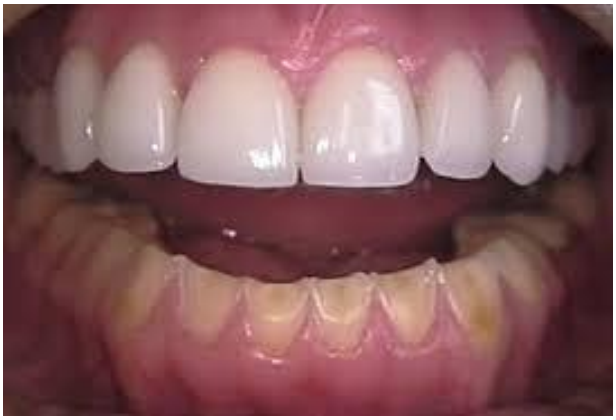
Prevention and treatment of erosion induced tooth wear

- When substance loss caused by erosive tooth wear reaches a certain degree, oral rehabilitation becomes necessary.
- As a result of the improvements in composite restorative materials, and in adhesive techniques, it has become possible to rehabilitate eroded dentitions in a less invasive manner.
- Therefore, the treatment options available to rehabilitate patients with erosion range from minimally invasive direct composite reconstructions to adhesively retained all-ceramic restorations [6].

Resin composite restorations (RCR), glass ionomer cement (GIC) and ceramic restorations are usually used [4]:

- If loss of Vertical Dimension <0.5 mm: Sealing or direct flowable Composite restoration is recommended.
- Loss of Vertical Dimension <2 mm: Direct Reconstruction with Composite Materials or glass ionomer restoration are recommended.
- Loss of Vertical Dimension >2 mm: Rehabilitation with indirect Ceramic Veneers and Overlays are recommended.
- Loss of Vertical Dimension >4 mm: Rehabilitation with indirect Ceramic restorations as crowns and bridges are recommended [4].

Figure 2. Severe loss in vertical dimension due to severe erosion in the lower teeth



Effect of erosive conditions on different tooth-colored restorative materials

1. Composite restorative materials

1.a. Effect of erosive conditions on microhardness and surface roughness of resin composite restorations [1]

- Nanocomposites are the most stable under erosive conditions with higher wear resistance and microhardness values. This is due to nano-sized regular particles, which allow the incorporation of a large volume of inorganic fillers.
- Surface roughness values of nanocomposites after erosive challenges are lower than hybrid composites due to homogeneous composition and their particles are less prominent on the surface.
- Immersion of micro-hybrid composites in hydrochloric acid (HCl, pH 2) or soft drink (pH 3.6) for 10 minutes, three times daily for 14 days decreased surface microhardness and increased surface roughness.
- The softening of the resin matrix of bisphenol-A-glycidyl methacrylate (bis-GMA) could be caused by leaching of the diluent agents such as triethylene glycol dimethacrylate (TEGDMA). This promotes displacement of the filler particles, contributing to the formation of a rough surface.
- Application of acidic products, such as acidulated fluoride compounds may led to an increase in toothbrush wear or loss of fillers of composite resin.

1.b. Effect of erosive conditions on adhesive bonding strength and microleakage of resin composite restorations [7]

- Composite specimens subjected to thermal/erosive cycling showed microleakage and decreased bond strength of etch- and-rinse and self-etching adhesives with no significant differences between them.
- In addition to dissolution of enamel and dentin margins. The effects on bonding are more pronounced on enamel than on dentin because erosion primarily affects the inorganic part of the tooth and bonding to enamel is mainly achieved by a micromechanical interlocking of resin into microporosities of the acid-etched surface. In contrast, the dentinal hybrid layer is composed of organic matrix, residual hydroxyapatite crystallites, and resin monomers.
- However, in case of GERD, the gastric protease (pepsin) leads to organic matrix degradation and progression of erosive lesions in dentin.

1.c Recent advances in composite resin restorations for treatment of erosive tooth wear [5]

- Recent improvements of the composite restorative materials make them suitable for indirect restorative procedures to rehabilitate worn dentitions.
- The CAD/CAM composite can be used to produce ultrathin occlusal veneers. Laboratory studies have shown decreased risk of failure of this conservative approach as compared to lithium disilicate ultrathin occlusal veneers.
- The CAD/CAM composite restorations behave similarly or even better than human enamel with respect to two-body wear and toothbrushing wear.

2. Glass Ionomer cement

2.a. Effect of erosive conditions on microhardness and surface roughness (Ra) of Glass Ionomer cement (GIC)

- Compared to resin composite, glass ionomer cement is more unstable and experiences a decrease in hardness values and an increase in surface loss under erosive conditions. This is due to the dissolution of the silicate-glass hydrogel network peripheral to the glass particles [1,8].
- Conventional low-viscosity GIC shows lowest microhardness and highest surface degradation compared to high-viscosity GIC and resin modified glass ionomer (RMGI) [1,8]. Moreover, conventional GIC does not provide enough protection against erosion for the surrounding enamel and dentin because it shows more marginal than bulk degradation.
- The RMGI shows gradual decrease of surface microhardness under acidic challenge, however, it is less susceptible to acidic degradation compared to conventional GIC, due to the presence of reinforcing resin within the matrix.
- Moreover, RMGI provides protection against erosion for the surrounding enamel and dentin and can be considered material of choice among fluoride releasing materials for restoring erosive lesions [9].

- However, the increase in the surface roughness of RMGI is due to the presence of glass particles, and possibly porosities, in its composition [8,9].

3. Ceramic restorative materials

The reconstruction of excessively eroded dentition opposing ceramic restorative materials is mandatory when there is need to restore the occlusal vertical bite, figure (3).

Figure 3. Severe erosion and attrition of maxillary incisors, Ceramic veneers for maxillary incisors fabricated on dies, maxillary incisors were restored with ceramic veneers luted with resin composite cement.

3.a. Effect of erosive conditions on microhardness and surface roughness (Ra) of Ceramic restorative materials

- Although ceramics have high chemical durability, strong acids such as HCl from gastric regurgitate (GERD) can etch the surface of glass-based ceramics, resulting in increased surface roughness and a decrease in the hardness values of the ceramic restorations.
- Zirconia is less reactive to the acidic environment [10].

N.B: Local hydrolysis in ceramic cracks is accelerated in acidic pH, as GERD, leading to crack propagation and, hence, ceramic corrosion. The subsequent increase in surface roughness can increase the accumulation of bacterial plaque on the ceramic restorations [10].

Conclusion

Ceramic and resin containing materials are effective in providing protection of enamel in advanced cases of erosion and can withstand the erosive environmental conditions. While the traditional GIC materials are susceptible to severe damage in patients experiencing strong citric acid or gastric acid induced erosion.

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Structure and Properties of Natural Biopolymers

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Abstract: Biopolymers are derived from polymers in which the prefix 'bio' refers to the living matter. They are produced by living organisms such as nucleic acids, polysaccharides, and amino acids and can be extracted from plants, or chemically synthesized from basic biological systems. Biopolymers are biocompatible (non-toxic), renewable, biodegradable because of the oxygen and nitrogen atoms found in their structural backbone, sustainable, eco-friendly, ease of handling, long-term stability, abundance, and simplicity of functionalization, Therefore, they are used in food, pharmaceutical, medical, and environmental applications. However, they have high production cost, ineffectiveness caused by the synthesis, development, and downstream processing processes.

Keywords: *natural biopolymers; biodegradation; collagen; chitosan.*

Definitions:

Degradable polymers are a broad term applied to polymers that disintegrate by physical, chemical, and biological mechanisms.

Biodegradable means that polymers will degrade under the enzymatic action of microorganisms into carbon dioxide and water which in turn are recycled in the nature.

Bio-based polymers are polymers derived from renewable resources such as plant sources[1].

Classification of biopolymers:

a) **According to the source of the raw materials and the biodegradability of the biopolymer [1]:**

1) **Biopolymers made from renewable raw materials (bio-based) and being biodegradable:** Such as poly (lactic acid) (PLA), Poly hydroxy alkanoates (PHAs), starch or proteins.
2) **Biopolymers made from renewable raw materials (bio-based), and not being biodegradable:** Such as polyamides from castor oil, and natural rubber.

3) **Biopolymers made from fossil fuels and being biodegradable:** Such as polycaprolactone (PCL).

b) According to the origin of the biopolymer:

1) Natural biopolymers:

- Polysaccharides such as cellulose, starch, and chitosan.
- Protein based biopolymers include albumin, gelatin, and legumin.

2) Microbial biopolymers: Poly hydroxy alkanoates (PHAs)

3) Chemically synthesized biopolymers: Poly lactic acid (PLA) and Polycaprolactone (PCL)[2].

Natural Biopolymers	Synthetic Biopolymers
• Biologically renewable. • Biocompatible (non-toxic). • Bio-adhesive material.	• Higher reproducibility. • Better mechanical and chemical stability. • Flexible in design and properties.
• Less stable. • Low melting point. • Structurally more complex.	• Less biocompatibility. • Expensive synthesis procedure. 6,7

Structure of Natural Biopolymers:

a) Polysaccharides:

- **Chitosan**: Chitosan is a straight chain polysaccharide that occurs naturally or can be obtained by deacetylation of chitin. Chitosan has reactive functional groups: amino and hydroxyl groups therefore, they have strong affinity with water and dilute acids, such as acetic acid, lactic acid, and inorganic acids. The solubility of chitosan depends on the concentration of amino groups. The amino groups of chitosan are highly reactive due to presence of free electron pair of nitrogen in the amino groups[3, 4]. The negatively charged surface of bacterial cells interacts with the positively charged amino groups in chitosan may cause damage to the cell wall and leakage of cell contents[3, 5]. Chitosan causes stimulation of inflammatory cells such as macrophages, fibroblasts and PMN neutrophils. Therefore, it could be used treatment of inflammation in the periodontium[3].

- **Hyaluronic Acid**

It is a linear mucoadhesive polysaccharide used in the preparation of gels for drug delivery and in wound healing by extracellular and epithelial regeneration. HA is characterized by ease of chemical functionalization, biodegradability, and hydrophilicity; therefore, it can maintain a humid environment and bond water molecules[6, 7].

- **Sodium Alginate:**

Alginate is a linear polysaccharide, a derivative of alginic acid. The main chain of sodium alginate contains many $–COO^-$ reactive groups. Therefore, it is used in drug and gene delivery, tissue engineering, wound healing, and taking oral impressions. It is characterized by biocompatibility, biodegradability, muco-adhesion, and low-cost production. However, it has poor mechanical properties and high degradation rate, therefore it could be combined with other polymers such as cellulose, chitosan and hyaluronic acid[8, 9].

- **Agarose:**

Agarose is a nondegradable polysaccharide. It is used in biomimetic remineralization. Agarose hydrogel can control the size and form of the hydroxyapatite crystal. It acts as a durable matrix for enamel rebuilding through interaction between the hydroxyl group of agarose and calcium, as well as providing a mineral reservoir for further remineralization. Moreover, agarose gel may be used as a scaffold for bone regeneration, especially when combined with hydroxyapatite (HA) or calcium carbonate ($CaCO_3$)[10, 11].

- **Cellulose:**

Cellulose is a high molecular weight (long chain) polysaccharide that is present in plant cell walls and could be produced by microorganisms. Each linear chain contains 1000-1500 glucose units. There are three hydroxyl groups in each unit. These hydroxyl groups interact with each other by intra and inter hydrogen bonding to form crystalline (ordered) regions. Cellulose is used in drug delivery systems because they are porous materials, which can facilitate the liquid uptake. Cellulose can interact strongly with water, thus swelling readily in water leading to its dissolution[12].

- **Gum Arabic:**

Gum Arabic is a dried, and gummy exudate from the stems and branches of Acacia Senegal. Gum Arabic has antibacterial activity *P. gingivalis* and *P. intermedia*. GA could improve dental remineralization and inhibit the formation of plaque, acting as a potential preventive agent in the formation of caries. Such effects are attributed to the high salt content of Ca^{+2}, Mg^{+2} and K^{+}. Incorporation of Gum Arabic improves the hardness of gypsum products. Small amount of Gum Arabic plus calcium carbonate added to the hemihydrate can reduce the amount of water required for mixing of both plaster and stone[6].

b) Protein based biopolymers:

- **Collagen:**

Collagen is one of the most abundant cellular matrix proteins. The basic structural unit of collagen is composed three polypeptide chain arranged in the form of a triple helix with two identical chains and the third differs in its chemical composition. Collagen presents in the gingival epithelium. It is used mainly to facilitate the process of healing[13]. Collagen membranes are also very useful for periodontal procedures of guided tissue regeneration. Collagen stimulates the differentiation and proliferation of osteoblasts and increases expression of bone morphogenic proteins which influences the regeneration of peri-implant and periodontal and improves the overall mechanical strength and stability of the regenerated tissue[14].

- **Fibrin:**

Glycoprotein present in human blood plasma characterized by porosity, deformability, elasticity and biodegradability, fibrin has great potential for application as a scaffold in tissue engineering. A fibrin matrix with entrapped cytokines, growth factors and cells, called platelet-rich fibrin (PRF) could be used in oral and maxillofacial surgery to improve bone healing, enhance new bone formation, and bone regeneration, and reduce pocket depth[15].

- **Gelatin:**

Biocompatible polymer with adhesive properties and high hemostatic activity used to improve the process of healing/regenerating damaged tissues, including post-extraction wounds. As a polymer

that promotes cellular attachment and growth but suffers from poor mechanical and antimicrobial properties, it could be used to create ideal wound dressing only after crosslinking with other polymers and the incorporation of antimicrobial agents e.g., gelatin-hyaluronic acid (HA) hybrid hydrogels[16].

- **Bone Morphogenetic Proteins (BMPs):**

Bone morphogenetic proteins (BMPs) are signaling molecules that are obtained from non-mineralized bone matrix. BMPs play an important role in regeneration and bone remodeling. They also increase bone response to alloplastic materials[7].

- **Silk:**

The raw silk thread produced by a silkworm is composed of core silk fibroin, and a glue-like coating consisting of sericin proteins. Silk fibroins possess high mechanical resistance. This is mainly due to strong hydrogen bonds (inter- and intra-chain) and van der Waals interactions generate a structure that is thermodynamically stable. Silk fibroin is in controlled drug delivery and in the production of three-dimensional porous scaffolds[17]. Combining PMMA with silk fibroins shows increased elastic modulus, tensile stress, and melting temperature[18].

Structure of Microbial Biopolymers:

- **Polyhydroxyalkanoates (PHAs):**

PHA polymers composed of short-chain-length monomers. Depending on the number of carbon atoms, PHAs are classified as short-chain-length PHAs that contain three to five carbon atoms and medium-chain-length PHAs that contain 6–14 carbon atoms. The PHAs are commercially produced by several bacteria as intercellular carbon and energy storage materials. PHAs can be processed by traditional polymer techniques for use in medical products such as surgical sutures, wound dressings, blood vessels, tissue scaffolds, surgical implants, and bone fracture fixation plates[1, 5, 19].

Properties of biopolymers:

1) **Density:**

Most biopolymers have higher densities than conventional polymers. The higher density values of biopolymers indicate higher energy and cost required for production[20].

2) Water sorption and Solubility:

Most biopolymers are more susceptible to the water sorption due to their natural source and hydrophilicity. For solubility, high crystalline biopolymers offer more resistance to dissolution in comparison to lower crystallinity biopolymers[21]. Water sorption is an essential property in rehydration and exudate absorption during wound-healing. Adequate moisture is mandatory for rapid treatment, preventing dehydration, bacterial proliferation, and infection[22].

Bacterial cellulose (BC) has a complex molecular structure, with water molecules bonded through hydrogen bonds. The BC fibers are composed of linear chains of glucan units linked through inter- and intramolecular hydrogen bonds, allowing BC to be mechanically robust while maintaining elasticity. Therefore, the free water (unbonded) can penetrate and exit the BC molecular structure[23].

3) Barrier properties:

Membranes or films are devices that promote the separation of a structure and the environment in which the structure is located such as wound dressing. Their objective is selective mass transport between both sides such as oxygen, water vapor, carbon dioxide and microorganisms[22]. Biopolymer films could be impermeable to both water vapor and oxygen. impermeability to water vapor but highly permeable to oxygen, or impermeable to oxygen and greatly permeable to moisture[21].

A wound dressing should be capable of free flow of oxygen to the wound which is essential for cell growth making the healing process faster. Increasing the hydrophilic nature of a polymer membrane increases water vapor permeation. Moreover, wound dressing material must have adequate bacterial barrier property to protect the wound from bacterial infection[24]. ***For example,*** polyvinylpyrrolidone (PVP)/ sodium-carboxymethylcellulose (CMC) hydrogel wound dressing has high rate of water vapor and oxygen permeability and performs as a good barrier for bacterial penetration[24].

4) Thermal properties:

One of the chief flaws of biopolymers is their tendency to easily deform under high temperatures[21]. Thermally instable biopolymer such as lignin should be incorporated with other polymers as blends, composites and copolymers thereby modifying the thermal properties[2].

5) Mechanical properties:

The mechanical properties depend upon the application of biopolymer. Applications, such as wound-healing dressings or tissue engineering require appropriate mechanical properties that can be achieved with plasticizer and crosslinking methods. In the case of dressings, flexibility is an important requisite in biopolymer films to improve the patient compliance and adaptation to the oral mucosa which is a very sensitive tissue (chitosan and pectin films). Addition of plasticizer increases the flexibility of biopolymer films. For tissue engineering, the mechanical properties of biopolymers films must be like the tissue to be repaired, crosslinking can be a useful tool to improve the tensile strength of biopolymers [22, 25].

Natural biopolymers are not suitable for applications that require high mechanical stress or load-bearing capacity. In contrast, synthetic biopolymers show better structural properties for load-bearing medical applications than natural polymers[26]. The modulus of elasticity and tensile strength is increased with a greater value of molecular weight. For example, PHAs are brittle, have low percentage elongation and tear strength because they are formed of short length chains[21].

6) Optical properties:

Some biopolymers are colorless and transparent such as starch-chitosan composites [2]. Bacterial cellulose composites containing silver nanoparticles that are used as wound dressing are transparent, allowing uninterrupted visualization of the wound without having to remove the dressing[23]. The crystalline structured materials showed more opacity compared to the amorphous structured materials. Transparency could be achieved by incorporating a transparent nucleating additive in the biopolymer matrix which tends to crystallize the polymer into a tremendously large number of crystals while maintaining a miniscule size lesser than the wavelength of visible light[21].

7) Biodegradability of biopolymers:

Biodegradability of biopolymers is a biochemical process, which involves hydrolytic cleavage of chemical bonds under specific ecological conditions by microorganisms or enzymes into their constituents and it might be aerobic or anaerobic[27]. In general, the biodegradation process could be biotic or abiotic. **Biotic degradation** occurs through enzymatic actions produced by organisms. While **Abiotic degradation** is the chemical and physical break down of the material, e.g., photodegradation, mechanical degradation, thermal degradation, and chemical hydrolysis under acidic or basic conditions. Biotic and abiotic degradation processes influence each other, mechanical degradation can for example lead to increased susceptibility of the polymer to enzymatic degradation, accelerating biodegradation[22, 28].

Biodegradation of biopolymers has many advantages and applications in tissue engineering and drug/gene delivery. Biodegradability of biopolymers makes them eco-friendly because they can maintain the environmental aspects in the presence of active compounds in the environment[27]. Conventional synthetic polymers might collect in the body, resulting in the degradation of toxic products[29].

- **Stages of biodegradation of biopolymers:**

1) Biodeterioration: breakdown the biodegradable materials into small pieces.
2) Depolymerization: the polymeric molecules are converted into lower-molecular-weight polymers.
3) Assimilation: Transported molecules are used as energy and carbon sources.
4) Mineralization: Metabolites may be excreted and reach the outside of the cellular medium[30].

- **Factors affecting biodegradation of biopolymers:**

1) The environment: The situations in which biodegradation processes happen are divided into two types of aerobic and anaerobic.
2) Other factors: chemical bonds, presence of microorganisms, temperature, wetness, oxygen accessibility, chemical conditions such as pH, and the molecular weight distribution of the polymer[27].

➢ **Aerobic biodegradation:** Occurs in the presence of oxygen in which the chemistry of the environment, system, or organism is characterized by oxidative conditions. For example, aerobic

biodegradation of lignin is an oxidative process carried out by lignin peroxidase as an extracellular enzyme in the presence of H_2O_2. Aerobic processes, unlike anaerobic processes, do not produce potent gases[27].

$$C_{Biopolymer} + O_2 \rightarrow CO_2 + H_2O + C_{Residue} + C_{Biomass}$$

- **Anaerobic biodegradation:**

Anaerobic process is a process in which there is no oxygen. Some biodegradable biopolymers are destroyed by the anaerobic process in the absence of oxygen. For example, cellulose degradation[27].

$$C_{Biopolymer} \rightarrow CO_2 + CH_4 + H_2O + C_{Residue} + C_{Biomass}$$

- **Enzymes for biopolymers biodegradation:**

These processes are the biotic side of the total decomposition of a compound. Several enzymes such as proteases, esterases, and glycoside hydrolases are involved, depending on the type of the bond to be hydrolyzed.

1) **Proteases:** Proteolytic enzymes (proteases) catalyze the hydrolysis of peptide (amide) bonds[31]. The amino acids glycine, proline and hydroxyproline base are hydrolyzed because of collagenase[32].
2) **Esterases:** Esterases are the most widely found enzymes in the nature. They help split of ester linkages by the addition of water[31]. The hydrolysis of ester bonds liberates the monomers which are transported and further digested through endoenzymes[28].
3) **Glycosidases:** Glycoside hydrolases cleave the glycosidic bond in polysaccharides such as starch (amylase), cellulose (cellulase), chitosan (chitosanase), and hyaluronic acid (hyaluronidases)[32].

8) Muco-adhesion property:

It is a multifactorial and complex property, essential for the success of orally administered pharmaceutical forms. Chemical (mucin adsorption) and mechanical (muco-adhesion strength) techniques are important to understand the muco-adhesion ability of biopolymers nanofilms used

as drug delivery systems for the oral mucosa. Chitosan and pectin biopolymers exhibit invitro muco-adhesion[25].Chitosan is the gold standard mucoadhesive biopolymer due to electrostatic interaction between its positively charged amine groups and the available carboxyl groups of mucins[25]. Pectin is another mucoadhesive biopolymer. The interaction between Pectin and mucin is driven by the formation of hydrogen bonds between their free carboxylic acid groups[33].

Modifications of Biopolymers structure and Properties:

1) **Crosslinking:**

Crosslinking reactions provide higher mechanical strength and improved stability by interconnecting molecules; however, crosslinking could cause reduced degradability and lower availability of functional groups in biopolymer[34].

Types of crosslinking:

Ionic Crosslinking through addition of divalent cations (e.g., Ca^{2+}) to the solution of biopolymer (e.g., alginate and pectin) enables the rapid formation of hydrogel. ***For example***, preparation of Interpenetrating polymer network (IPN) hydrogel, which relied on Ca^{2+} cross-linking between alginate chains and hydrogen bonding interaction between polyvinyl alcohol (PVA) chains[9].

Hydrophobic interactions through heat-induced gelation of proteins (e.g., milk protein) which is based on the denaturation and coagulation[35].

Hydrogen bonding that is formed upon cooling of a heated aqueous solution of biopolymer (e.g., agarose) below its gelation temperature. This approach is used in the encapsulation of biomolecules/cells without the necessity of chemical crosslinkers or initiators that can lead to undesired interactions with the bioactive agents[35].

For example, Hydroxyapatite become uniformly distributed throughout the agarose upon cooling, the agarose solution sets into a gel in which chain segments are stabilized by hydrogen bonding, unlike the cross-linking of alginate which is limited by the chemical crosslinkers concentration[36].

Chemical crosslinking reactions through covalent crosslinking of reactive functional groups of biopolymers. Covalent bonds produce strong and permanent networks compared to physical interactions, covalently crosslinked biopolymers exhibit enhanced mechanical properties, colloidal stability in vivo conditions, few by-products and high specificity and selectivity[35].

Examples, Glutaraldehyde can react with functional groups in both proteins and carbohydrates and shows improvement in tensile properties. Although glutaraldehyde provides good improvement in mechanical properties, contradictory evidence has been provided on the cytotoxicity of glutaraldehyde-crosslinked materials. Cytotoxicity of glutaraldehyde is dependent on the concentration used, and up to 8% glutaraldehyde was shown to be non-cytotoxic[34].

Carboxylic acids such as citric acid could be used to crosslink and improve the mechanical properties and stability without compromising the cytocompatibility. Crosslinking biomaterials with citric acid provide pendant functionality and allows formation of ester bonds leading to increased availability of binding sites for bioconjugation[34].

Photo-crosslinking and enzymatic crosslinking approaches are used for in situ gelation of biopolymer due to the rapid gelation (normally no more than 10 min) via strong covalent bonding at ambient temperature[35]. To avoid the undesirable changes and possible side effects of chemical crosslinkers, photo-crosslinking have been used. Collagen films are crosslinked with a combination of glucose and UV irradiation which generates free radicals that form reactive, linear glucose molecules and enhance crosslinking[34].

Regarding the reaction catalyzed by enzymes, an oxidation reaction catalyzed by tyrosinase, or peroxidase is one of the main enzyme-mediated cross-linking methods. These enzymes oxidize substrates to reactive forms, which have the potential to make covalent bonds. Also, transglutaminase or sortase make bonds between specific amino acids, are examples of enzyme-mediated reactions used in hydrogel fabrication[37].

Natural crosslinkers such as proanthocyanidin (PA) found in grape seeds increases the thermal resistance and resistance to enzymatic degradation of collagen films after crosslinking, without affecting their cytocompatibility. Several weeks after subcutaneous implantation, the PA-crosslinked membranes showed considerably higher penetration of fibroblasts without any disintegration of tissue[38].

2) Composites:

Material Composite material consists of two or more materials that behave together to get the better properties. Biopolymer/ceramics composite scaffolds are imitations of natural bone.

Hydroxyapatite, as the mineral part (osteoconductive function) is used in the formation of composites with collagen, gelatin, chitosan, chitin, elastin, PCL, PLLA, and PGA can be the matrix phase for the bone replacement[39].

3) Blending:

Blends composed of a mixture of two or more biopolymers and a mixture of biopolymers with synthetic polymers to modify their properties. Blending is a cost-effective technique in which the components can be combined in a molten state or can be solubilized in the same solvent to form a homogeneous material through hydrogen, ion, and dipole bonds. Miscibility of the components has a key impact on the properties of the blend such as single glass transition temperature and show intermediate mechanical properties between those of the two constituents[40]. Blending synthetic and natural polymers provides a control of the degradation rate of the system as the degradation kinetics of a polymeric blend increases on increasing the amount of the natural polymer, the blend composition can be adjusted to make the scaffold degradation rate match the growth rate of the regenerating tissue[39].

Examples:

- A blend between PCL and starch has good mechanical properties and enzymatic degradation[39].
- Chitosan-gelatin (CS/G) coatings to a Titanium surface supports osteoblasts attachment, migration, and proliferation. Moreover, new bone formation around CS/G implants occurs at 8 and 12 weeks[41].
- Nano sized cellulose imparts higher stiffness to the nanocomposites even at low concentration when incorporated in polymer matrices due to their ability to form interconnected network structures through hydrogen bonding. thus, its incorporation in chitosan matrix can improve mechanical properties of chitosan[42]. Chitosan blended with cellulose nanofiber showed better physical characters and stability which made them useful in pharmaceutical applications[20, 42].

4) Graft copolymerization:

Grafting is the process of incorporation of new and desired properties biopolymers without affecting the basic properties of the polymeric backbone. Reactive functional groups in the chemical structure of biopolymers, including hydroxyl, carboxylic acid and amino groups act as sites for grafting to which monomers are covalently reinforced onto the polymer chain[43, 44].

Methods of grafting:

- Grafting initiated by chemical method (free radical uniting and ionic uniting).
- Grafting initiated through the radiation method
- Photochemical grafting method
- Enzymatic grafting method (e.g., tyrosinase in protein biopolymers)
- Plasma radiation-induced grafting[44].

Example:

Graft copolymerization of cellulose with ethyl acrylate monomer (chemical free radical grafting) reduces the water absorptivity and improves the heat stability, moisture, chemical, and thermal resistance[43].

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