**Introduction** (1 page)

A very significant clinical problem, which we face nowadays, is bone injuries and defects, which are due to trauma, osteoporosis, and tumors. Most of the people find it difficult to be healed naturally and they must undergo multiple surgeries for recovery. Therefore, bone tissue engineering has become a highly promising tool to tackle the most challenging bone related clinical issues.

In bone tissue engineering, the biodegradable substitutes act as a temporary skeleton inserted into the defective sites of skeleton or lost bone sites, in order to support and stimulate bone tissue regeneration while they gradually degrade and are replaced by new bone tissue.

A good understanding of the bone anatomy, properties, and internal organization will ensure ideal selection of biomaterials with optimal characteristics for bone tissue regeneration.

Biomaterials have been used for bone regeneration for many years and have played a critical role in improving the quality of life for patients suffering from bone defects or injuries. Biomaterials for bone regeneration are materials that can be implanted into the body to stimulate the growth of new bone tissue or to replace damaged or diseased bone tissue.

Bone is a complex tissue with a hierarchical structure, composed of cells, extracellular matrix, and mineralized tissue. The ideal biomaterial for bone regeneration should mimic the structure and function of natural bone, and promote the formation of new bone tissue without inducing inflammation or adverse immune reactions.

**Bibliographic part**:(10-13 pages)

**- Généralités :**

Bones are complex structures that performs many functions for the body: Firstly, they provide support and shape to the body, allowing it to stand upright and bear weight. Secondly, they protect vital organs such as the brain, heart, lungs, and spinal cord from injury and damage. Thirdly, bones enable movement by providing attachment points for muscles. Fourthly, bones act as a mineral reservoir for important minerals such as calcium and phosphate, which are essential for bodily functions like muscle contraction, nerve transmission, and blood clotting. Finally, bone marrow, the soft tissue within bones, produces blood cells including red blood cells, white blood cells, and platelets (Lee and Einhorn, 2001).

Bones are classified as long bones, short bones, flat bones, irregular bones, structural and sesamoid bones. The long bones, such as the femur and humerus, are tubular in shape and are found in the arms, legs, fingers, and toes. They contain bone marrow, which produces blood cells. The short bones, such as the wrist bones and ankle bones, are roughly cube-shaped and are found in the hands and feet. Flat bones, such as the skull bones, scapulae, and sternum, are flat and plate-like, and provide protection for the organs they cover. Irregular bones, such as the vertebrae and facial bones, have complex shapes that do not fit into any of the other categories. Sesamoid bones are usually small, round and flat. They are found near joints of the knees, hands and feet. Structural bones are small, flat, oddly shaped bones found between the flat bones of the skull (Lee and Einhorn, 2001). Figure (1)

Une image contenant diagramme

Description générée automatiquement

Figure 1 : Classification of bones by shape (“BONES AND SKELETAL TISUES,” n.d.)ref

All bones have an exterior layer called cortex that is smooth, compact, continuous, and of varying thickness. In its interior, bony tissue made up of intersecting trabeculae, which vary in amount in different bones and enclose spaces filled with [blood](https://www.britannica.com/science/blood-biochemistry) vessels and marrow.

The hard outer layer of bones is composed of cortical bone, which is also called compact bone as it is much denser than cancellous bone. The cortical bone gives bone its smooth and solid appearance, and accounts for 80% of the total bone mass of an adult human [skeleton](https://en.wikipedia.org/wiki/Skeleton) (Lee and Einhorn, 2001). It is a very dense material with 5 to 10% porosity (Ogueri et al., 2019).

It consists of multiple microscopic columns, each called an [osteon](https://en.wikipedia.org/wiki/Osteon), it is the primary anatomical and functional unit of compact bone. the diameter of each osteon is between 0.1 and 1mm and its maximum length is 1cm. The columns are metabolically active (Biga et al., 2019).

Each column is multiple layers made of collagen and calcified matrix and is called a lamella (plural = lamellae) or Haversian lamellae, which are concentrated around a central canal called the [haversian canal](https://en.wikipedia.org/wiki/Haversian_canal) which contains blood vessels, nerves, and lymphatic vessels. These vessels and nerves branch off at right angles through a perforating canal, also known as Volkmann’s canals, which connect the osteons together. Figure (2).

Cortical bone is covered by a [periosteum](https://en.wikipedia.org/wiki/Periosteum) on its outer surface which is a tough fibrous membrane, and an [endosteum](https://en.wikipedia.org/wiki/Endosteum) on its inner surface. The endosteum is the boundary between the cortical bone and the trabecular bone (Biga et al., 2019).

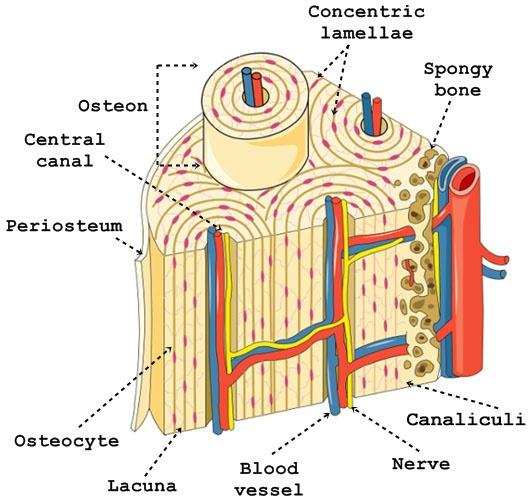


Figure 2 : Structure of cortical bone ref

Trabecular bone, or spongy bone, also known as cancellous bone, it is mostly located inside flat bones, such as the sternum, skull bones, pelvic bones, and vertebrae. It is also found in the ends of long bones such as the femur and humerus, where it serves as a reinforcement for compact bone. Spongy bone plays several important roles in the body. First, it is responsible for the production of blood cells, as it contains red bone marrow, which produces red blood cells, white blood cells and platelets. Additionally, it is involved in bone resorption and formation, in response to stimuli such as physical activity and hormonal changes. It also serves as a reinforcement for compact bone, absorbing shock and distributing pressure over the entire surface of the bone (Lee and Einhorn, 2001).

Unlike compact bone, which is dense and rigid, spongy bone has a more porous and less dense structure, with a high [surface-area-to-volume ratio](https://en.wikipedia.org/wiki/Surface-area-to-volume_ratio). This makes it weaker and more flexible. Trabecular bone is highly [vascular](https://en.wikipedia.org/wiki/Vascular), It is made up of small ossicles or "trabeculae" which are the primary anatomical and functional unit of cancellous bone, these trabeculae form a network of interconnected channels and cavities.

The spaces between the trabeculae called lacunae, which contain bone cells called osteocytes and are filled with red bone marrow, which produces blood cells and stores nutrients needed for bone formation. The lacunae are linked together by tiny channels, called canaliculi, which allow osteocytes to communicate with each other and with blood vessels (figure 3). They also allow nutrients and metabolic wastes to move between the osteocytes and the blood vessels that are found in the marrow spaces (Biga et al., 2019).

Trabecular bone accounts approximatively for the remaining 20% of total bone mass. This percentage could be changed due to many factors (Lee and Einhorn, 2001).

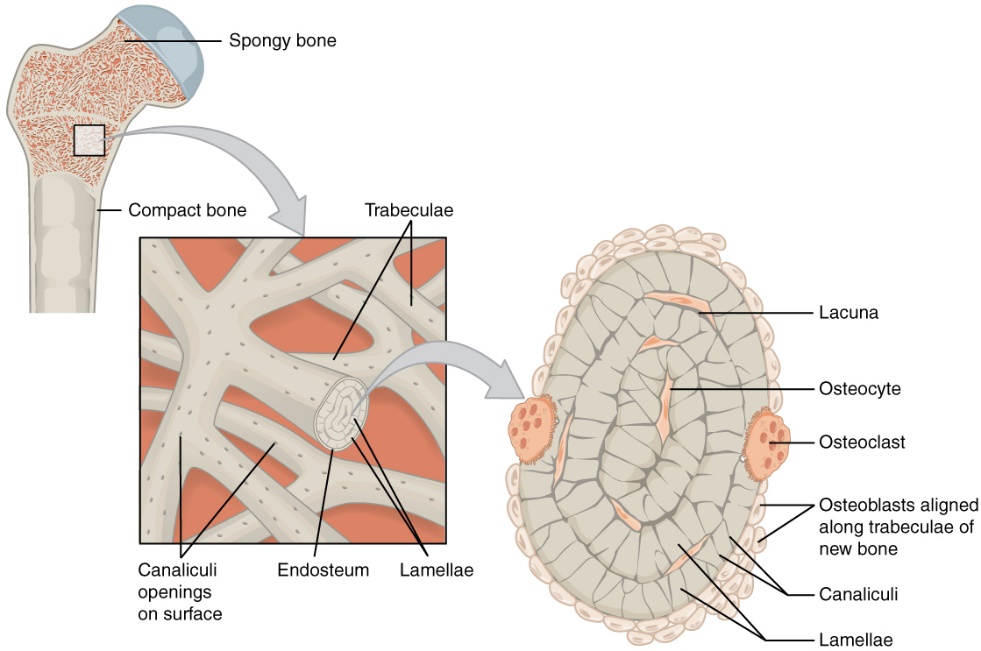


Figure 3: Structure of trabecular boneref [What is the Difference Between Compact and Trabecular Bone - Pediaa.Com](https://pediaa.com/what-is-the-difference-between-compact-and-trabecular-bone/)

The extracellular matrix consists of an organic (osteoid) and an inorganic phase. By weight, approximately 70% of the tissue is mineral or inorganic matter, water comprises 5 to 8%, and the organic or extracellular matrix makes up the remainder. Approximately 95% of the mineral phase is composed of a specific crystalline hydroxyapatite having the nominal composition of Ca10(PO4)6(OH)2 and the 5% remaining of the inorganic phase contains other minerals, including magnesium, sodium, and potassium, which contribute to its overall mineral density and mechanical properties (Boskey and Robey, 2013). Ninety-eight percent of the organic phase is composed of type I collagen which is a fibrous protein constructed in the form of a triple helix of of three chains composed of approximately 1000 amino acids each linked by hydrogen bonds and covalent bonds to create a strong and durable bone tissue (Lee and Einhorn, 2001). The triple helices then come together to form fibers, which can be very long and which give collagen its strength and durability. In addition, there is a variety of noncollagenous proteins, including osteocalcin, osteopontin, and bone sialoprotein. These proteins play diverse roles in bone development, mineralization, and remodeling. The proportions mentioned before, are changing depending on age, species, and site (Boskey and Robey, 2013).

These different components have both mechanical and metabolic functions. In generally the mineral phase, provides toughness and rigidity, while the organic matrix provides tensile strength and flexibility to the bone (Ficai et al., 2009). [Furthermore](https://www.merriam-webster.com/thesaurus/furthermore), there is an electrostatic interaction between the carboxyl groups (COO-) of collagen and the positive calcium ions (Ca2+), which strengthen the bone structure and gives it its mechanical resistance (Katti et al., 2010).

Bone is an anisotropic material with mechanical properties that are dependent on the orientation at which the forces are applied. The compressive moduli of cortical bone and trabecular bone are in the range of 17–20 and 0.02– 0.9 GPa, respectively. The compressive strengths of cortical bone and trabecular are 100–230 and 2–40 MPa, respectively. The tensile moduli of cortical bone and trabecular bone are in the range of 7–30 and 0.05–0.1 GPa (50–100 MPa), respectively. The tensile strengths of compact bone and trabecular bone are 80–150 and 1–10 MPa, respectively (Ogueri et al., 2019).

Bones are not static tissue but need constant maintenance and remodelling. There are [three](https://www.ncbi.nlm.nih.gov/books/NBK537199/) main cell types involved in this process.  Osteoblasts can range in size from 10-30 micrometers (µm) in diameter. They are responsible for generating and repairing bone. They [produce](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/osteoblast) a protein mixture composed primarily of collagen (osteoid), which is mineralized and becomes bone. In addition, they produce hormones that play a role in the mineralization of the matrix. Osteocytes have a more elongated shape than osteoblasts with 15 to 30 μm in length and 10 to 15 μm in diameter. They are inactive or mature osteoblasts that are mineralized and remain within the bone they have created. They have macroreceptors that allow them to receive mechanical input signals and transmit these stimuli to other cells in bone. (“Bone - Bone morphology | Britannica,” 2023). Osteoclasts are bigest cells with multiple nucleus, with a diameter greater than 100 µm. They [use](https://www.ncbi.nlm.nih.gov/books/NBK537199/) acids resulting from certain reactions to break down used bone. This process is called resorption. They dissolve the minerals in bone and release them into the blood. These phenomena of bone formation and resorption occur under the effect of different hormones and mechanical stress (Lee and Einhorn, 2001).

Simple bone fractures tend to heal spontaneously within weeks, but in more complex cases such as tumor resection or comminuted fractures, the bone healing process may be very slow or even impossible. This situation is called a critical size bone defect. In the clinic, these critical size defects are treated by implanting bone grafts. There are three types of bone grafts: allogeneic, autologous and xenogenic.

The first bone substitutions are thought to have been made in the 5th century; these were bone allografts made from bone tissue taken from recently deceased individuals. When we are using an allogeneic bone graft, the bone used for the transplant comes from a human donor. This type of bone graft requires a close match between donor and recipient, and there is a risk of transplant rejection (Ferré et al., n.d.) (Chiarello et al., 2013).

In an autologous bone graft, the bone used for the graft is taken from the patient's own body. This can be done from the bone of the hip, tibia or another part of the patient's body. **Autologous bone grafts are often considered the safest and most effective method of bone grafting**, as the risk of rejection is zero. They have optimal osteogenic, osteoconductive and osteoinductive properties and do not cause an immunogenic reaction. However, there are also some potential drawbacks to using autologous bone grafts. The procedure to harvest the bone can be painful and may require a longer recovery time. In addition, there may be limited availability of suitable donor bone if the patient has already undergone previous surgeries or has certain medical conditions (Laurencin et al., 2006).

the third type of bone graft is Xenogenic bone graft, the bone used for the graft comes from another animal species. This type of bone graft is rarely used because of the high risk of graft rejection and infection (Ferré et al., n.d.).

The success of a bone graft depends on several factors, including the type and location of the bone injury, the size of the graft, and the patient's overall health.

Biomaterials (organic or inorganic) with desired properties that can mimic the original tissue structure become a popular area in bone tissue regeneration, to overcome the drawbacks of allografts and autografts.

**- Biomaterials for bone replacement :**

Biomaterials (organic or inorganic) with desired properties that can mimic the original tissue structure become a popular area in bone tissue regeneration, to overcome the drawbacks of allografts and autografts.

European Society for Biomaterials defined in 1986 what it completed in 1991, during the conference in Chester (UK), a biomaterial as « a non-living material, of natural or artificial origin, used in a medical device, and designed to interact with biological systems, whether it is part of a medical device for diagnostic purposes or a tissue or organ substitute or a functional replacement (or assistance) device».

For bone regeneration, the biomaterial must exhibit specific features such as biocompatibility which is a critical property of biomaterials used for bone regeneration. It refers to the ability of the biomaterial to not produce toxic responses when placed within the body, to avoid any rejection or inflammation that can impede the healing process. Biodegradability is a critical factor that must be considered, because it allows the biomaterial to be replaced by new bone tissue over time. It must degrade at a rate that corresponds with the rate of new bone formation. If the implant degrades too fast and if not enough bone is formed, it will break again. The implant should integrate into the surrounding tissue (osseointegration), should promote the cell attachment, proliferation and migration of osteoblastic cell lines (osteoinductivity). Osteoconductivity refers to the ability of the biomaterial to support bone ingrowth and provide a scaffold for new bone formation. It enables the biomaterial to integrate with surrounding bone tissue and support the regeneration of new bone. Porosity is another important property. A biomaterial with the appropriate pore size (which shall be correlated with the dimensions of bone cells and other functional units within bone tissue) and distribution allows for nutrient and cell transport, which promotes new bone growth and can facilitate the growth of new bone tissue within the material and promote vascularization, which is essential for bone healing. Another requirement for scaffolds porosity is pore interconnection (the existence of access routes between pores which encourage the penetration of bone cells and blood vessels). The mechanical strength of a biomaterial is critical for its success in bone regeneration applications. Biomaterials used for load-bearing applications must have sufficient mechanical strength to support the load-bearing demands of the bone. The biomaterial must also be able to maintain its structural integrity during the healing process, as new bone tissue forms and replaces the biomaterial (Yu et al., 2015).

Three major classes of biomaterials are used to fabricate scaffolds: metals, ceramics and polymers. Metals, possesses excellent biocompatibility and high mechanical performance, and it releases non-toxic ions (e.g., titanium and its alloys). However, poor corrosion resistance could induce tissue reactions and raise the risk of loosening. The higher elastic modulus of metals relative to natural bone can also result in a therapeutic failure. In addition, poor biodegradability may lead to further impairment of tissue ingrowth. However, surface modification has been applied to improve bioactivity in traditional biomaterials. It enhances metallic corrosion resistance and promotes osteoblast attachment through coating, showing superior osteogenesis and integration ability. Stainless steel is sometimes used for bone regeneration. While it is strong and inexpensive, it can cause an immune response and may not be biocompatible for all patients (Zhang et al., 2022).

Ceramic biomaterials, have a similar composition to natural bone and can provide structural support for bone growth. The two most common bioceramics used are, Hydroxyapatite (HA) that has excellent biocompatibility and osteoconductivity and can be made into porous structures that allow for cell infiltration and vascularization. However, HA is brittle and can fracture under stress, and it may not be suitable for load-bearing applications. The second one is Tricalcium phosphate (TCP), it is biocompatible and can be resorbed by the body, making it a good option for temporary scaffolds. However, like HA, it can be brittle and may not be strong enough for load-bearing applications.

Lastly, polymers are widely used in bone regeneration and are generally classified as natural or synthetic. Many of them have demonstrated good mechanical properties, biocompatibility and biodegradability.

Synthetic polymers offer a versatile alternative to create 3D constructs for bone regeneration, because of their biocompatibility and their tailorable biodegradation. The most used are polyfumarates, polylactic acid (PLA), polyglycolic acid (PGA), PGA (PLGA), and polycaprolactone. Furthermore, open porous structures can be obtained from these polymers. They can be processed by various methods including electrospinning, gas foaming, rapid prototyping, or three-dimensional printing to generate a range of three-dimensional scaffolds with different porosities and surface characteristics.

PLA is a thermoplastic polyester which has excellent mechanical strength, processability, biocompatibility, good degradation rates, and nontoxic degradation products. In spite of this good properties, it suffers from the lack of ideal surface chemistry that could aid cell adhesion and proliferation (Ogueri et al., 2019). Polycaprolactone (PCL) is a biodegradable polymer that is often used for bone regeneration using different methods as Solvent casting and porogen leaching, electrospinning (ES) and 3D printing. It has a good mechanical mechanical properties and biocompatibility. However, PCL exhibits a longer degradation time (2–3 years) as other biomaterials and is degraded by microorganisms or by hydrolysis of its aliphatic ester linkage under physiological conditions (Dwivedi et al., 2020). Poly(lactic-co-glycolic acid) (PLGA) scaffolds can be processed into 3D porous structures that can be designed to fit bone defects. They are also biodegradable and biocompatible. However, clinical application of pure PLGA scaffolds for bone regeneration is hampered by poor osteoconductivity and inflammatory responses that originate from the production of acidic by-products on PLGA degradation (Lanao et al., 2013).

Although synthetic polymers have their benefits, they also come with drawbacks, namely their poor cell attachment and migration, as well as the acidifi cation of neighboring tissues during degradation (Donnaloja et al., 2020). In contrast, natural polymers such as proteins (e.g., collagen, silk and elastin) or polysaccharides (e.g., cellulose, chitosan and starch) are of special interest due to they beneficial interactions with cells, do not release acidic degradation products and their biological and chemical similarities to natural tissues.

Collagen is a natural protein that is a major component of the extracellular matrix of bone tissue. It is biocompatible and can be made into porous structures that promote cell adhesion, proliferation, and differentiation and tissue regeneration and providing strength to the tissue. Nevertheless, they owe insufficient bioactivity to foster the cell bone forming ability and poor mechanical strength to sustain bone regeneration, often making it necessary to add polymers and other biomolecules in order to improve osteoinductivity (Filippi et al., 2020).

The most popullar collagen composite used in bone regeneration is collagen-hydroxyapatite composite. hydroxyapatite provides strength and rigidity. Collagen- hydroxyapatite composites are often used as a scaffold due to their similarity to natural bone, as well as their ability to promote cell attachment, proliferation, and differentiation (Wahl et al., 2007). Lee et al used a combination of collagen with synthetic polymers, e.g. PLGA and PCL to increase the low Young modulus value of collagen (Lee et al., 2006).

Another type of protein which is Gelatin, is a natural protein derived from collagen. It can be easily processed into the desired shape, including hydrogels, films, and sponges, and can be combined with other materials to form composites for bone regeneration. Due to its biocompatibility, biodegradability and its low immunogenicity. Singh *et al.* presented a 3D gelatin/hyaluronan/alginate (GHA) blend that was freeze-dried and then cross-linked with calcium chloride (CaCl2). The implantation of this scaffold in mice demonstrated pronounced osseointegration, recruitment of cells and reduced inflammatory response compared to controls (Singh et al., 2014). Linh *et al.* developed fiber mats composed of polyvinyl alcohol (PVA)/gelatin loaded with various amounts of biphasic calcium phosphate (BCP) nanoparticles. Studies in rats showed an increase in bone formation with the 50% PVA/gelatin-50% BCP blend, indicating its potential use in bone regeneration (Linh et al., 2013). Gelatin is still limited with its disadvantages such as, low degradation and limited availability, Gelatin is derived from animal sources, which may limit its availability for use in certain applications.

Polysaccharides are carbohydrates which are composed of sugar molecules (monosaccharides) joined together by the glycosidic linkages. Polysaccharides have seen a massive demand for use as biomaterials. some of the most studied polysaccharides for bone substitution include chitosan, hyaluronic acid, cellulose and starch.

Chitosan has been found a fascinating candidate in bone substitution application due to its unique biological properties including biocompatibility, biodegradability to harmless products, nontoxicity, remarkable affinity to proteins and antibacterial. Generally, chitosan has three types of reactive functional groups, an amino group as well as both primary and secondary hydroxyl groups. These groups allow modification of chitosan like graft copolymerization, which can produce various useful scaffolds for tissue engineering applications. The chemical nature of chitosan in turn provides many possibilities for covalent and ionic modifications which allow extensive adjustment of mechanical and biological properties. Chitosan has been shown to degrade in vivo, which is mainly by enzymatic hydrolysis. The final degradation products are biocompatible. Chitosan can be easily shaped into various forms like sponges, films, fibers, beads, and more complex structures. Chitosan has poor mechanical properties and high sensitivity to water. Its properties are generally enhanced by combining it with other components.

(Hsieh et al., 2005) choose a γ-poly(glutamic acid) (γ-PGA), a hydrophilic and biodegradable polymer, to modify chitosan matrices to produce a γ-PGA/chitosan composite biomaterial.. with interconnected porous structure with a pore size of 30–100 μm. water absorption rate, and swelling ratio were improved by adding γ-PGA to the matrices. Additionally, the mechanical strength of the porous γ-PGA/chitosan matrices was about 25–50%, higher than that of the unmodified chitosan matrices. The cell density on the 20% γ-PGA-modified matrices was almost triple that on the unmodified chitosan matrices on day 5. These composites were found to be an appropriate environment for cell attachment and proliferation.. It was proved that are very promising biomaterials for bone tissue engineering applications.

Acid Meyer and Palmer were the first to isolate hyaluronic acid (HA) in 1934 from the vitreous humor of the eye [161]. There has been an emerging interest in the biomedical field since its discovery

HA belongs to the family of glycosaminoglycans which are linear polysaccharides consisting of alternating units of N-acetyl-D-glucosamine and glucuronic acid.

[Hyaluronic acid](https://www.sciencedirect.com/topics/chemistry/hyaluronic-acid) a natural polymer found in the human body, is often used to stimulate extracellular matrix microenvironments to promote cell activities such as adhesion and proliferation. Furthermore, HA is capable of cross-linking with other polymers and entrapping drugs/growth factors to achieve controlled release.

HA alone shows weak mechanical properties and is degraded by hyaluronidase. To improve the scaffold's strength and bioactivity, chemical modification and combination with other materials are often required.

(Nguyen and Lee, 2014) fabricated a novel bone substitute to enhance bone healing by combining Hyaluronic acid–Gelatin hydrogel biphasic calcium phosphate ceramic, and the resulting scaffold. The fabricated scaffold showed high interconnected porosity, a significant increase in cell proliferation with an average compressive strength of 2.8±0.15 MPa, which is usually recommended for cancellous bone substitution.

The natural polysaccharides are favorable for aerogel formation. An aerogel is a porous ultralight material derived from a gel, which is prepared via dissolution of a polysaccharide, solution gelation followed by drying in which the liquid component for the gel has been replaced with a gas using different drying techniques such as, supercritical (aerogels), freeze-drying (cryogels), vacuum (xerogels). Aerogel has outstanding characteristics such as high surface area, huge porosity and low density making it potential for wide range of applications (El-Naggar et al., 2020). Bioaerogels have low density (0.02–0.2 g/cm3) and rather high specific surface area (200–600 m2/g). They are highly compressible without breakage up to strains of 70–80%. The properties of bioaerogels can be tuned due to a large amount of hydroxyl groups on polysaccharide chains which can be functionalized (Soorbaghi et al., 2019).

starch aerogels emerge as an attractive alternative for bone scaffolds, where the advanced properties of aerogels are supplemented by the biocompatibility, the complete physiological degradation, and the abundance of starch in nature (Santos-Rosales et al., 2020).

Starch is one of the most imperative natural polymer used in medical applications due to its low cost, renewable nature and ability to degrade into various environments without releasing toxic products. Starch incorporates two macromolecules: amylose and amylopectin. The latter one is responsible for material’s crystallinity. The molecular chains are organized to form alternative amorphous and crystalline regions. Amylose and amylopectin have different physiochemical properties which impact on the overall properties of the starch.

….

**Advancement part** (environ 15 pages)

**Conclusion** (1 page).

**References**

The physical and chemical properties of this mineral have been determined by a variety of techniques including chemical analyses, X-ray diffraction, vibrational spectroscopy, energy dispersive electron analysis, nuclear magnetic resonance, small angle scattering, and transmission and atomic force microscopy(Boskey and Robey, 2013)

The surface properties of a biomaterial can play a critical role in its success in bone regeneration applications. The surface should promote cell adhesion and differentiation, which facilitates new bone formation. The surface properties can also influence the interactions between the biomaterial and surrounding tissues, which can impact the healing process. While surface characteristics affect bioactivity and adhesion of cells on the surface of composites,

All these 5 functional units are grouped in micrometric units named “starch grains” which are available in plants such as potato, rice or wheat. Various starch characteristics such as composition, grain interaction or swelling ability, depend on the extraction source. It has been reported in the literature that starch with higher amylose content improved the different properties such as tensile strength, elongation, impact strength and tear resistance of polymeric films. The starch gelatinization/melting is primarily determined by the mechanism of interaction with water in aqueous media. As the water molecules penetrate within the starch granules, the material is organized in an amylose gel with amylopectin-rich granules.

Gelatinization depends on the quantity of water available in the solution: smaller water quantities will not ensure an adequate swelling for gel forming while excess water may lead to a separation between the amylose gel and the amylopectin crystallites. Starch gelatinization is also influenced by temperature and shear forces which increase molecules mobility and allows faster destruction of crystalline regions. Despite its advantages, the use of starch is limited by the processing difficulties, poor mechanical properties and water-sensitivity to name a few. These are currently overcome by the adequate choice of additives and/or chemical modifications that shall maintain its long-term stability. Also, a better property control is ensured by combining starch with other materials for preparing starch blends (with other polymers) or starch composites (among which the most studies are the ones based on starch and phyllosilicates, clays and other polysaccharides).

Une image contenant diagramme

Description générée automatiquement<https://www.frontiersin.org/files/Articles/532791/fbioe-08-00474-HTML/image_m/fbioe-08-00474-g004.jpg>

Hydroxyproline residues in collagen can form hydrogen bonds with the phosphate groups of hydroxyapatites. The last one is about covalent bonds Une image contenant texte

Description générée automatiquement. The trabeculae are aligned towards the mechanical load distribution that a bone experiences within long bones such as the [femur](https://en.wikipedia.org/wiki/Femur). . In mature bone, trabeculae are arranged in an orderly pattern that provides continuous units of bony tissue aligned parallel with the lines of major compressive or tensile force. Trabeculae thus provide a complex series of cross-braced interior struts arranged so as to provide maximal rigidity with minimal material. The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to direct forces out to the more solid compact bone providing strength to the bone.

The pores or spaces within spongy bone, which are also called trabeculae, are not randomly oriented. Rather, their orientation follows the lines of stress and tension that the bone is subjected to during normal physiological loading.

Specifically, trabeculae in spongy bone tend to align themselves along the lines of mechanical stress, known as stress trajectories. These stress trajectories are determined by the direction of loading forces that are applied to the bone during daily activities, such as walking or running. The orientation of the trabeculae can be influenced by various factors, including the direction and magnitude of forces, the location within the bone, and the hormonal and mechanical signals that regulate bone remodeling.

In general, the trabeculae in spongy bone are oriented in a way that maximizes their resistance to compression and minimizes their resistance to tension. This means that the trabeculae are aligned perpendicular to the lines of compressive stress, which are typically oriented along the long axis of the bone. Meanwhile, the trabeculae are oriented parallel to the lines of tension, which are typically oriented transverse to the long axis of the bone.

The orientation of pores in spongy bone is important because it influences the mechanical properties of the bone, such as its strength, stiffness, and resilience. In particular, the alignment of the trabeculae can affect the bone's ability to resist fractures, absorb shocks, and distribute loads, making it an important consideration in the study of bone biomechanics.

**Biomaterials for bone replacement" (6-7 pages) :**

Deux paragraphes sur les matériaux utilisés pour la régénération osseuse,( et je propose de rajouté ici les proprietes exiges pour ces biomatériaux cad de mentionner que le matériau doit avoir une tel porosité, doit etre osteoconducteur, biocompatible,...) en précisant vers la  fin que je vais être focalisée sur les polysaccharides.

Ensuite Décrire ce qui existe pour chaque type de polymère et les mélanges (procédé de fabrication et propriétés , avantages et desavantages).

un paragraphe concernant les biomateriaux a base d'amidon pour la regeneration osseuse, pour justifier le choix d'aérogel en amidon + structure d'amidon & définitions d'aérogels.