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A review on Biodegradable Materials for utilization in Orthopaedic Implantsand Biomedical Applications

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Abstract

The environment in which a biodegradable material will be used must be compatible with it that is, it must not produce harmful components before dissolving beyond the specified period and must degrade at acceptable rates. In orthopaedic applications, the primary aim of such materials is to eliminate the need for secondary surgery.Biodegradable materials, such as biodegradable alloys, currently offer higher biocompatibility as well as mechanical and biodegradation characteristics.Although there is a lot of work being done with biodegradable materials and biodegradable implants for orthopaedic applications these days, it has been discovered that maintaining optimal material degradation so that the bone tissues can be completely regenerated (while healing) after a fracture is very difficult. The implant is designed to provide the best mechanical qualities and degradation rates possible. Biodegradable materials have several advantages over non-biodegradable biomaterials, including 1) better biocompatibility and non-toxic behavior, 2) the ability to degrade in-situ, 3) improved bone healing, and so on. Several biodegradable alloys are employed in orthopaedic applications. Numerous biodegradable materials, such as metals, ceramics, and polymers, are being examined for this application, according to a recent study and research. This review focuses on biodegradable materials and optimizing mechanical properties, degradation rates, and the healing process.

Keywords:Biodegradable, Implant, Degradation, Bio-compatibility, Mg-based alloys

1. INTRODUCTION

Nowadays, bone fractures are very commonin which a bone gets completely or partially broken or damaged because of injury because of gradual load, cyclic load, or impact load [1]–[4].Bone is a living tissue that is mostly composed of calcium phosphate[5]–[7].Human bone after getting fractured has shown self-healing phenomenon when it is placed in the right place, some type of fractures can be supported by outside which is called non-invasive and its examples are plaster, strap, splint, etc. but some cases are very serious in which internal support is required by the help of surgery[1], [8], [9].

One of the two categories of implant materials are non-biodegradable implants or conventionally utilized materials (such as stainless steel, titanium, etc), which requires a second surgery because the material does not get dissolved and the secondcategory of implant materials are biodegradable material which eliminates requirement of secondary surgery and some of its examples are polymers, ceramics, magnesium alloys, etc. [5], [10], [11], Conventionally used bio-materials such as titanium, stainless steels, etc are required to be detached from body following a further surgery that allows the bone to heal completely [12], [13] and it causes extra healthcare cost and mental stress to the patient [10], [14], [15]. Also, conventionally used non-biodegradable materials have shown poor biocompatibility and also produce toxic materials [16], [17].

Biodegradable materials are in continuous demand in recent times and a lot of work is going on in this field because it also eliminates the problem of stress shielding, stress shielding is a situationthat occurs when the weight is shared by the implant rather than the bone as a result of which density of the bone after healing is not optimum and hence bone tissue is not regenerated properly [1], [5], [18].

Biodegradable materials are in demand because they are compatible, non-toxic, have better mechanical and biological properties, eliminate secondary surgery, adequate degradation rate[1], [19], [20].

In Fig. 1 a broken femur bone is shown in which an Implant or fixator will be applied and it will get healed after some time automatically.

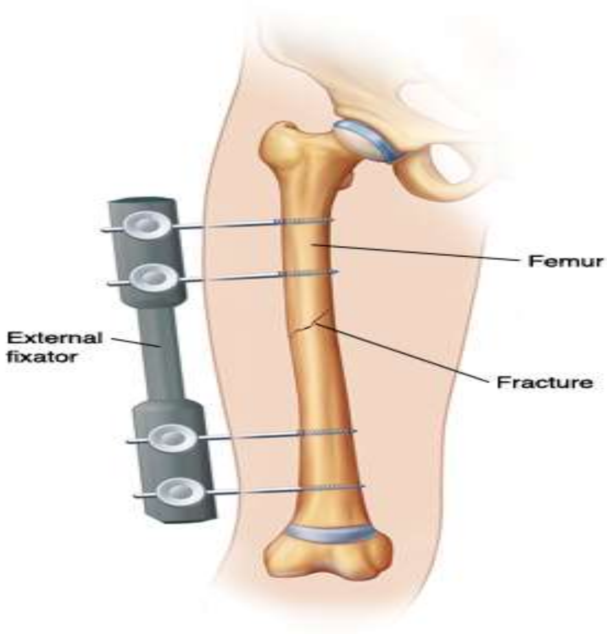

Fig.1 Broken femur bone with External fixator/Implant

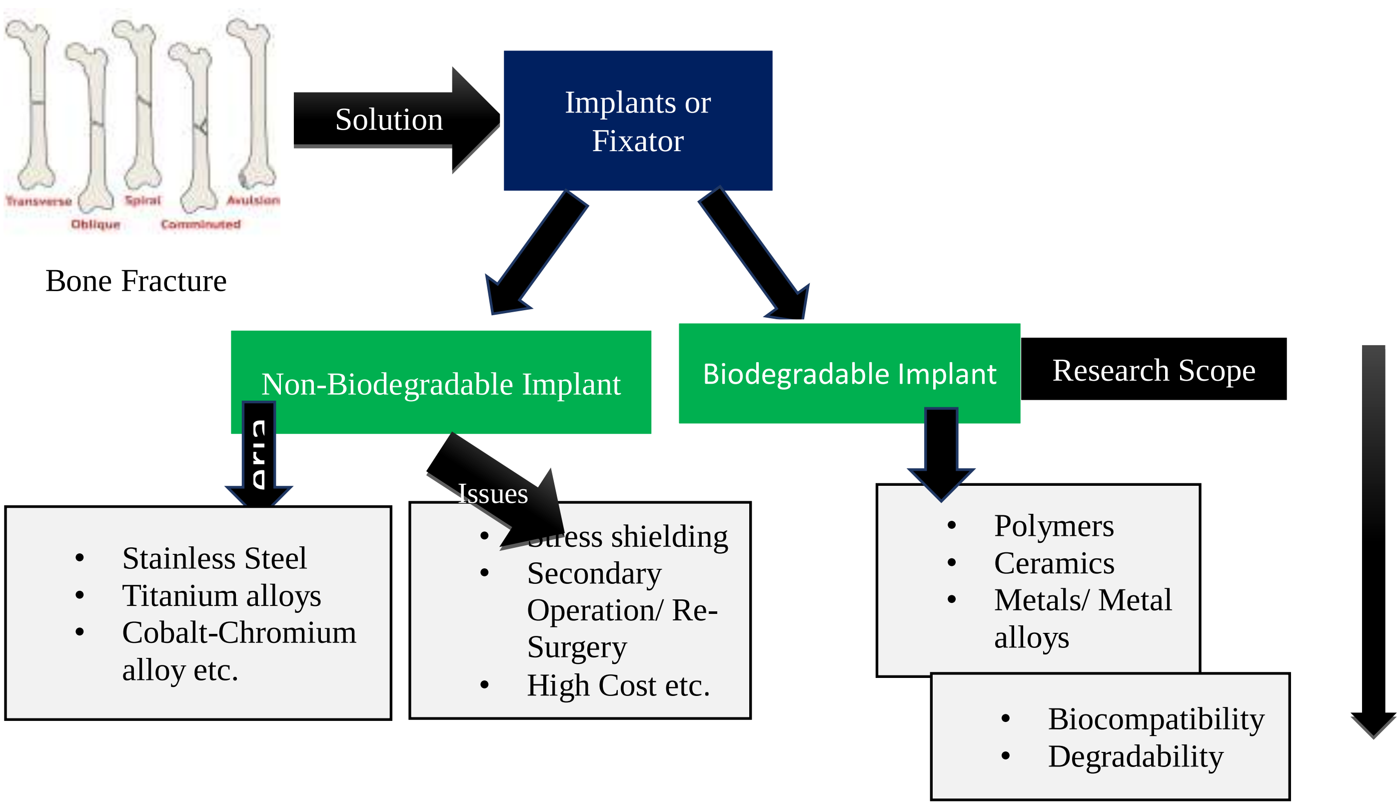

Fig.2 Flow chartrepresenting the difference between non-Biodegradable and Biodegradable Implant and Research scope with Biodegradable Implants

In Fig. 2, a schematic flow chart is presented showing the difference between Non-Biodegradable and Biodegradable Implants. Inthis chart issues with conventionally used Non-Biodegradable Implants are shown and the research scope associated with Biodegradable Implants is also presented.Table 1 lists the characteristics of several forms of bone.

Table 1. Properties of different types of human bone[21], [22]

Material type	Compressive Strength (in MPa)	Tensile Strength (in MPa)	Young's Modulus (in GPA)	Elongation (in %)	Total Strength Loss (in Months)
Human cortical	130–225	35–284	16–20	1.071–2.10	None
Human cancellous	6–10	1.5–38	0.05–0.1	0.5–3	0.5–1

2.BIODEGRADABLE MATERIALS

Biodegradable materials should breakdown or corrode gradually in vivo or in vitro with the proper host response, and should entirely disintegrate inside the body following complete healing of the fractured bone without releasing hazardous compounds[10], [23].
Biodegradable materials can be classified as:

2.1 Polymers

Polymers are macromolecular materials consisting of long and repeated chains of molecules. Polymers have unique properties depending on the type of molecules and their binding characteristics[5], [24].
Biodegradable polymers are one of the most commonly used for bone fracture repairing. Modifications in structural composition and manufacturing methods can alter the corrosive behavior of polymeric materials[5].But there have been some concerns about the acidic products of PLA such as low strength and inflammatory reaction[12].
Some examples of Biodegradable polymers are PLA (polylactic acid), Collagen, Chitosan, etc[5].

2.2 Bioceramics

They are used as an alternative to metallic biomaterials. They are biocompatible but have shown poor fracture toughness, brittleness, and less strength.
Some examples of bioceramics are Tricalcium phosphate, HA (hydroxyapatite), Dicalcium phosphate, etc. [5]

2.3 Biodegradable metals and alloys

The most commonly utilized metals in biomedical applications include stainless steel, titanium, and chromium cobalt alloys but these materials have shown poor biocompatibility, cytotoxicity and require secondary surgery [8], [14], [16].
Due to these limitations, the ideal implant should be biocompatible and biodegradable, with mechanical properties that are identical to the bone. The density of Mg and its alloys is 1.74–2 g/cm3, which is alike to that of naturally occurring bone.Mg-based implants have the same elasticity modulus as a natural bone and are osteoconductive, biocompatible, and biodegradable[16], [21], [25], [26].
However, the rapid breakdown of Mg after implantation is a major disadvantage that limits its widespread usage in medical applications[25], [27]. Various methodologies and advanced procedures have been used throughout the years to control the rate of degradation until the bone has healed completely so that the implant maintains its mechanical integrity.This has been a major concern for biomedical engineers and metallurgistsand they are trying to figure out how to make implants that can degrade in a regulated manner. The most successful and effective way of regulating the pace of deterioration of magnesium composites was discovered to be alloying elements in the Mg matrix[14], [28], [29].
Fast degradation rate, localized corrosion mode, and inferior mechanical characteristics are all major difficulties with Mg-based alloys, which must be addressed earlier than they may be used as biomaterials. Grain refinement could help with property enhancements.In an active environment, the refining reduces corrosion resistance; yet, in an encouraging passive environment, it increases resistance to corrosion. In simulated human scenarios when inert reactivity occurs, smaller particles might favor lower rates of uniform corrosion. The anticorrosive characteristics of magnesium alloys were improved by coating the surfaces with a more stable oxide layer with finer grains[30]–[32].
Some mostly used examples of biodegradable metals are:

1) Mg-based
2) Calcium-based
3) Zinc-based
4) Strontium-based
5) Manganese-based
6) Lithium-based
7) Zirconium-based

2.3.1 Magnesium

Implants are typically made of biocompatible metallic implant materialsbecause of having superior mechanical strength, wear resistance, and corrosion resistance. However, because of the stress shielding effect, chronic inflammatory reactions, etc are caused by the use of Magnesium based implants which can result in the need for a secondary surgery[8], [10], [14].Therefore, a biodegradable metallic implant made up of magnesium (Mg), zinc (Zn), and iron (Fe) have been produced. Mg is mixed with other metals to make alloys for increasing the strength and reducing its faster degradation rates.Mg is also a necessary component of the human metabolic system, serving as a cofactor for a variety of enzymes and assisting in the integrity of DNA and RNA. As a result of these commonalities[21], [33], [34], Mg is a suitable option for biodegradable metal material due to its good biocompatibility.Table 2 lists the characteristics of many types of Mg-based biodegradable alloys.

Table 2: Properties of different Mg-based alloys[8], [33], [35]

S. No	Mg – alloy	Ultimate tensile strength (in MPa)	Yield strength(in MPa)	Elongation (in %)
1.	Mg-1Ca	238	136	12
2.	Mg-3Zn	231	131	-
3.	Mg-1.5Sr	80	41	2.61
4.	Mg-4Zn-0.55r	170	105	3.05
5.	Mg-1Zr (rolled)	179	131	17.51
6.	Mg-Zn-Mn (extruded)	281	245	22.5
7.	Mg-3Li (as extruded)	170	95.5	12.31
8.	Mg-3Li-2Zn (as extruded)	211	114	18

Zinc, manganese, calcium, and rare earth elementsare commonly utilized as magnesium alloying elements.Magnesium deteriorates as a result of corrosion. Byproducts include magnesium, magnesium hydroxide, and hydrogen gas[1], [36], [37]. Other elements can be employed to alter the rate at which a magnesium alloy deteriorates. Because of the presence of intermetallic and impurities in the second phase, pitting and localized corrosion are thought to be implicated in the degradation of Mg alloys[38]. The alloy's breakdown rate is influenced by pH, temperature, blood plasma, and proteins, in addition to the alloy itself. Magnesium alloys have also been subjected to surface modification and surface treatments to slow down the deteriorating process[25], [39].

2.3.2 Calcium

The most commonly employed element as a biomaterial is calcium, which is primarily stored in human bones. In Mg, Ca has a solubility limit of 1.34 weight percent[40], [41]. In terms of bone formation, resistance to corrosion, and mechanical properties, Mg with 0.61–0.70 percent Ca offers the best results[41]. AZ91-Ca, which contains calcium and magnesium, had significantly greater corrosion resistance than AZ91[42]. As the Ca concentration grows, the thicker and coarser Mg_2 Ca phase precipitates along grain boundaries, decreasing the Mg–Ca alloy's mechanical characteristics and corrosion resistance. An overabundance of calcium in the kidneys causes stones[43].As a result, calcium levels of less than 1% should be maintained.

2.3.3 Zinc

The nutrient-dense element that can be found in all of the body's organs and tissues is Zn. The combination of zinc with magnesium increases its mechanical qualities and resistance to corrosion[44]. The reduction in H_2 generation is the most effective result of Zn inclusion[45].The grain size is reduced and the mechanical properties are enhanced when up to 3% Zn is added to a binary Mg alloy [46]. Increasing the Zn concentration in a ternary Mg–Zn–Ca alloy raises the tensile strength from 104 MPa to 182.5 MPa and the rate of elongation from 41 to 90 percent[47]. The Mg–3.0Zn–1.0Ca alloy has been discovered to be the best for biomedical applications. When 16 percent Zn is added to Mg–0.6Si, tensile strength, elongation rate, and resistance to corrosion all improve [48]. Zn enhances the ultimate tensile strength of the Mg–3Ca–2Zn alloy by 21 percent [40].When the Zn level exceeds 3 wt.-percent, Zn-rich particles attack the fracture start sites. Excessive quantities of Zn above a certain threshold, if taken, might be harmful to the body [46].

2.3.4 Strontium

Chemical, ecological, and metallurgical similarities exist between magnesium and strontium. By enhancing bone mass and lowering the risk of fractures, Sr improves bone growth and aids in the treatment of osteoporosis[49]. The inclusion of Sr to magnesium alloys enhancesthe refinement of the grain andprevents corrosion[50]. Due to their low rate of corrosion and moderate mechanical attributes, Mg–2Zn–0.5Sr and Mg–0.4Zn–0.5Sr have been proposed as feasible biodegradable materials[51].Mg–2Sr alloy had the strongest strength and the slowest rate of corrosion among hot rolled Mg–Sr binary alloys with Sr concentrations ranging from 1.05 to 4.05 wt. percent. Increased Sr concentration over 2% reduces the resistance to corrosion of Mg–Sr alloys[52]. However, for biocompatible Mg-based implants, less than 1% Sr is recommended.

2.3.5 Manganese

Manganese is a crucial micronutrient for human health[53], and it helps Mg alloys resist corrosion without impairing their mechanical qualities [54]. Manganese is commonly found in ternary alloys with other metals such as magnesium. The addition of 1% zinc to an Mg–Mn alloy increases its anticorrosion properties. Introducing Mn to an Mg alloy improves resistance to corrosion while reducing impurity consequences. Mg–2Zn–0.2Mn was investigated for corrosion in the Ringer physiological solution[10].After 168 hours of exposure, the corrosion resistance of Mg–2Zn–0.2Mn alloy was four times that of AZ91 alloy because of the $Mg(OH)_2$ layer's superior protective characteristics.Mg–Zn–Mn alloys exhibit good mechanical characteristics[14]. After 18 weeks in an in-vivo study, approximately 54 percent of the as-cast Mg–12Mn–1.0Zn implant had decomposed, even though magnesium degradation did not cause a rise in serum magnesium levels or renal issues after 15 weeks. Mn is restricted to less than 1% by weight in Mg-alloys[53].

2.3.6 Lithium

Mg–Li-based alloys are becoming more suitable for stents due to their high ductility and ability to meet the requirements of radically expanded stents[55]. The inclusion of Li decreases the Mg-alloy lattice's axis ratio (c/a), making it easier to activate prismatic slips and enhancing deformability[26]. As a result, mechanical processing methods such as rolling and extrusion are frequently used to enhance the microstructure of Mg–Li alloys[46].Lithium has no deleterious impact on cell viability in in-vitro investigations [56]. A thorough investigation of the biocorrosion characteristics, biocompatibility, and mechanical properties of Mg–Li-based alloys for cardiovascular stent usage is still to be accomplished.

2.3.7 Zirconium

Zr is mostly used as a grain refiner in Mg alloys [57]. In-vitro and in-vivo, Zr has superior biocompatibility and osseointegration [58].In ternary Mg alloys, Zr is the most beneficial element.When 1% Zr was added to Mg, it increased mechanical properties [59].The damping properties of Mg-alloys get improved by the addition of Zr, which may aid in vibration and stress absorption at the implant site.The Mg–1Zr–1Ca alloy as-cast has an ultimate tensile strength of roughly 125 MPa and an elongation to failure of about 8%. In general[51], the Zr alloying percentage in biomedical magnesium alloys should be less than 0.8% by weight[48].

A table comparing the properties of bone with other materials is shown in table 3. Magnesium-based alloys have characteristics that are similar to bone, as shown in this table and hence it can support proper healing stages of the bone also it can eliminate problems associated with non-biodegradable implants. However, magnesium has shown faster degradation rates and so it can result in degradation of the implant before the healing of bone thus, this problem should be resolved and it can be resolved by alloying pure magnesium with other biodegradable materials such as Zinc, HA, etc.

Table 3. Comparison of properties of Materials[1], [8], [60]–[62]

Tissue/ Implant material/ Alloy	Density (g/cm3)	Ultimate strength (MPA)	Yield strength (MPA)	Elongation (%)	E (Modulus of Elasticity) (MPA)
Bone	1.80-2.10	110-130	104-121	0.7-3	15-25
Stainless steel	7.8	490	190	40	200
Titanium alloys	4.43	950	880	14	113.8
Pure magnesium	1.74-2.0	90-190	65-100	2-10	41-45
Pure zinc	5.4	33	-	16	9.1

3. BIOCOMPATIBILITY

A medical device's biocompatibility is described as the material's good performance in biological applications combined with a good host response in live systems[63]. To be employed in biomedicine, a biodegradable implant must be biocompatible. Biocompatible materials have been discovered and tested in metals, ceramics, and polymers; Magnesium alloys with calcium

phosphate coatings can enhance biocompatibility and resistance to corrosion. They could be used in biodegradable implants in the future [1], [46].
Biocompatibility is measured using both in vivo and in vitro tests[39].

4. BIODEGRADATION PROCESS AND CORROSION TESTS

Some biocompatible metals possess a biodegradability feature, which enables them to break down in vivo in a physiological environment with time[64].Biocompatibility and biodegradability are remarkable for magnesium, zinc, and other commonly used biodegradable metals[1].
Biodegradable materials' corrosion behavior is extremely sensitive to the harsh environment. Corrosion rates were observed to vary by a factor of 100 based on the diverse components of solutions, such as buffer and protein. Hank's solution, minimum essential medium (MEM), and solutions supplemented with different amounts of fetal bovine serum (FBS) were employed as test solutions[65].
Weight loss and volume loss with time are often used methods in the in vivo model to determine deterioration rates (few days to one year)[66]. It must be removed from the insertion site and scanned for good resolution in 3-D micro-CT scans, which may then be converted into an equivalent corrosion rate. In-vitro degradation rates are affected by the time frame (10 hours to 18 weeks) as well as the solution (SBF, Hank's, etc.)[1].
The in vitro degrading properties were assessed using electrochemical measurements and immersion tests in a simulated body fluid (SBF).

5. CONCLUSION

From an engineering and biological aspect, developing biomaterials for bone regeneration devices and prosthetics is a difficult task. Degradable materials for fractured bone healing are being actively researched and generate a lot of attention in the development of biomaterials investigation since their biodegradable nature allows patients to avoid a second operation and save money and time. Natural and synthetic polymers, as well as bioceramics, already are in clinical application, whereas magnesium-based metals are a novel class of biodegradable materials under study.Different biomaterials have different mechanical qualities, biological behavior, and biodegradation mechanisms. In comparison to polymers and bioceramics, magnesium alloys have a higher tensile strength and stress elongation. Ceramic materials have the highest amount of brittleness. From a biological standpoint, it has been proved that bioceramics and magnesium alloys heal and generate more new bone than polymers.One of the most essential properties of degradable biomaterials is the rate and amount of degradation. Metals and alloys containing magnesium as a component corrode in body fluid at a rather fast rate at first, then gradually slow down over time. Because their core structures stay constant, the mechanical strength of magnesium alloys does not deteriorate with degradation. Due to their inherent limitations, traditional metallic prostheses made of non-biodegradable materials are quickly becoming outdated.

Implants made of biodegradable materials are helping to eliminate unpleasant and time-consuming additional surgery procedures aimed at removing or replacing the implant. A full study of all stages, from raw material selection to fabrication, is essential to properly treat all types of defects, fissures by the application of biodegradable implants. The study and forecast of bone-biodegradable-implant interface performance reveal that while developing a biodegradable-implant, a balance of mechanical, degradation, and biological behavior must be considered.

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