Scope, development, application of magnesium as bioresorable material

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Abstract

Magnesium is proving itself as a new generation metallic biomaterial which has the natural ability to biodegrade itself due to corrosion when made to interact with human tissues along with aqueous body fluid to treat, improve or replace anatomical elements of the human body. Magnesium based implants serves as temporary scaffold when they are placed in vivo and vitro which acts as temporary support for the part to be healed and was found that the healing took at a faster rate. After a deep search studying and observing different study work it was found that these implants were physiologically compatible, nontoxic, cytocompatible and stimulates bone growth with other favorable characteristics. Magnesium based alloys are very much helpful in different structural body parts such as orthopedic, dentistry, cardiovascular, craniofacial, otorhinology. Main concentration of this review was to discuss some of the more commonly available and frequently used methods for development of bio implant materials and their strengthening mechanism. This review work puts a light on the summary of magnesium based material development for different biomedical applications, with their biocorrosion behavior with advantages, weaknesses and characteristics, as well as a biological translation for these results. This will help the new researchers, scientists, scholars to find a better light material as bioimplant which are in them biodegradable and reduces the pain of secondary surgery. Copyright © 2018 VBRI Press.

Keywords: Biomaterial, scaffold, physiologic, craniofacial, cytocompatible.

Introduction

Bio materials are the material used for repairing and giving initial temporary support to the diseased or infected tissues. It interacts with the human body tissues, body fluids to improve and replace the anatomical elements of the body. They are also known by the name of implants which are inserted in the human body to perform some specific function. The use of biomaterials started around 4000 years ago by the ancient Egyptians for closing the wounds with the help of linen threads, after that Europeans made the use of sutures made from catgut. Inca surgeons used to repair cranial fractures with gold plates and for artificial teeth ancient Mayans used sea shells. Lan in 1895 performed the first surgery for the fixation of bone with the help of metal plates, early developmental stages faced the problems such as corrosion and insufficient strength with the time and increase in knowledge and advancement people became more interested about the behavior of metals with the human body which lead to increase in demand of materials for bio medical applications. During world war II, a physician, Sir Harold Ridley observed that pieces of destroyed cockpit canopies which were embedded in the eyes of pilots were well tolerable and the word biocompatibility was coined which lead to the invention of intraocular lenses made of polymethylmethacrylate. Over half of the twentieth century the use of different metals for medicals implants increased and physicians gained a better understanding about the behavior of body to implants. Invention of stainless steel was a kind of miracle which changed the application of metals as implants and medical devices, it solved the major problem of corrosion and was able to provide good strength and increased life to the part. This new material gained interest and attracted the clinicians **[1-3]**.

Different types of materials are now used for different clinical applications for various parts of the body. Some major materials are stainless steel, titanium, nickel, magnesium and others. **Table 1,** shows the application of materials in different fields with the part used to make the body function proper.

Table 1. Metal implants for different applications **[4]**.

Field of Application	Components of implant
Orthopedic	Artificial joints
	Bone fixation, Pin, Screw, Plate
Dentistry	Orthopedic wires
	Fillings
Cardiovascular	Artificial valve
	Stents
Otorhinology	Artificial ear drum

Acceptability of bioimplant

The most important requirement of a bioimplant is its acceptability in the body; it generally depends on three factors shown in **Fig. 1.**

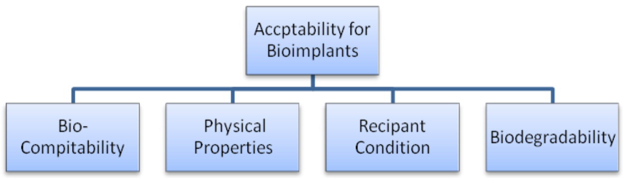

Figure. 1. Acceptability of bioimplant material.

Biocompatibility

Biocompatibility is understood as a long term implantable material or device which is biologically non reactive and inert chemically, it should be non toxic, non allergic and can perform its function smoothly without showing any negative effect when it is placed in the needed medium or surrounding, it should not affect the tissues and restrict the cause of cancer. It was observed in the study that the bioimplanted material can not possess properties like bone conductivity, blood compatibility, bioactivity, and other biofunctionalities by themselves and for improving the properties needed some modifications in the metallurgy **[5,6]**. This problem was somehow solved by applying a coating of biopolymers for blood compatibility, coating of hydroxyapatite bioactive ceramics for bone conductivity **[4]**.

Physical properties

Properties play a crucial role in selection of material and are an important factor for acceptance of the material by the body. There are different properties which are to be looked but out of them three major properties are:

(a) Mechanical property

(b) Chemical property

(c) Tribologoical properties

Some of the mechanical properties are strength, ductility, yield strength, elastic modulus, fatigue resistance, hardness, and surface finish, corrosion resistance which provide temporary support and help in healing the injured part in the set time period. These properties are derived from its type, design, processing methods, composition of the alloy and thermo mechanical treatments **[2]**. Chemical properties define the behavior of the implanted material and the reaction in the implanted material and the surroundings **[4]**.

Recipient condition

It has been seen that human body in itself is a complex system which reacts differently for every single body. It consists of different body parts some of them are soft and some hard which are shown in **Table 2**. Interaction with blood and other body fluids present in the human body are some difficult conditions of the host **[2,4,7].**

Table 2. Different hard and soft tissues of the body.

Hard tissues	Soft tissues
Cortical bone	Articualr cartilage
Enamel	Fibro cartilage
Cancellous bone	Ligament
Dentine	Tendon
Bones	Skin
Skull	Blood vessels
	Intraocular lens

Biodegradability

Biodegradability is the property of a material to degrade itself after a required time period without producing any adverse or toxic effect on the host material and surrounding. Biodegradable material constitutes a good class of biomaterials which support the healing process of the diseased tissue. It has a positive interaction with the physiological site of implantation **[6]**. Degradable materials are proposed from polymers and metals, as metals are considered more suitable bioimplant material and it is a new concept for the world. Metals play an important role in our body as they are the part of necessary minerals required by the body for health growth. Magnesium and its alloys have been investigated by the various research scholars and scientist as density of magnesium is nearby same as the natural human bone and can easily be degraded and can be simply excreted by simple excretion processes. The concept of biodegradable material aroused because it was observed in the studies that some implants were needed for very short time to just provide temporary support for the infected part, while it was much better option if the implanted material could get degraded itself expelling the secondary surgery done to remove the implanted material and would decrease the healing time, as the biodegradable material helps in stimulating the tissue growth of the infected part. These interventions were applied for specific cases such as orthopedic, cardiovascular, and pediatric field. **Fig. 2,** shows the temporary biodegradable stent used for opening the narrow and blocked artery **[8-10]**.

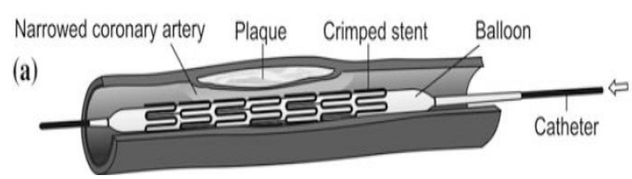

Fig. 2. Biodegradable stent used for cardiovascular surgery **[8].**

The concept behind different bioimplant materials is same, however it has different physiological working environments with some specific functions to be performed for example:

(a) Stent is used for opening and clearing the blocked artery to provide regular supply of blood and other body fluids, for this artificial stent is used generally of magnesium and its alloys as they do not require secondary surgery and degrade itself and performing its function.

(b) Screw and pins are other bioimplant materials which degrade on them self after application. They are used for joining the fractured bone to provide temporary support to the broken or fractured bone and other orthopedic applications.

The degradation of the biomaterial should be at slower rate depending on the healing time of the infected part it should not get eroded before complete healing process and the degradation process should not be so fast that the degraded material gets accumulated near the implant or get collect at other body parts which can cause some other body problems. The degradation rate should be such that the amount of degraded material is removed from the body in regular time intervals **[11]**. These degraded particles should be transported easily through the body. It is very difficult to obtain a perfect life span of a bioimplant material as human bodies act differently for every single body a rate of healing varies from body to body, for obtaining the life span of bioimplant material different in vivo and vitro tests are done to get the optimum results.

Parameters for bioimplant material selection

A bioimplant material must provide long term service without any harmful affects on the body, for this a set of parameters need to be fulfilled to get the best results and easy functioning of the diseased part. Some of the major Parameters are response to host which decides how the implanted material will behave in the host and its surroundings, does it produce any adverse effect or not in different working conditions. Biomaterial which is implanted in the body tissue should be non toxic, its path biology and tissue structure needs to be studied properly for proper functioning, biofunctionalities is another important factor to be looked over as the implanted material have to perform its specific function within in the range and required time period without any adverse effect on the surrounding. Some of the implanted part and devices are shown in **Table 3** with its function to be performed in human body **[2-4]**.

Table 3. Shows the implanted part and device with its function in the human body.

Implant	Function
Artificial heart	Controls blood and fluid in the body
Artificial bone	Stress distribution
	Load transmission
Pacemaker	Electrical stimulation
Cochlear implant	Regulates transmission of sound.
Artificial knee joint	Articulation to movement of joint.
Cosmetic surgery	Filling the injured space

Different types of materials are used for making bioimplant these materials are generally classified as metals and non metals. Metals in combination with other metals form alloys to make an implant part, while non metal is further classified into polymers, ceramics and composites as shown in **Fig. 3**. With this **Table 4**, shows different materials used for making biomedical implant materials and devices.

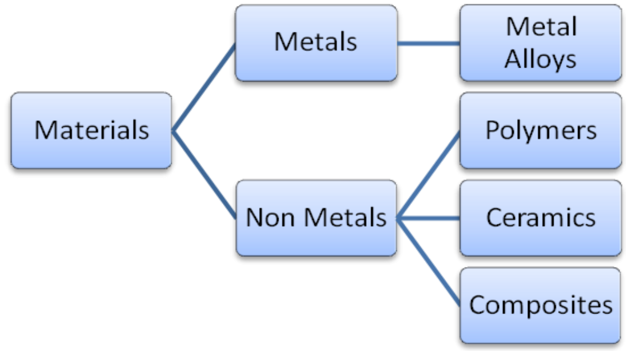

Fig. 3. Shows materials for bio implant.

Metals for biomedical applications

It is seen that major elements in periodic table are metals. Metallic implants are being used from 17th century. In 18th century first metal screw as implant was used during surgery. Metallic implants are generally used for places where load and stiffness is an important factor. Different metals are used like magnesium, titanium, chromium, molybdenum, silver gold and others in their pure form and alloys which are further discussed in brief of the study material.

The type of material used depends on the part of application, properties and behavior with the human body. Some major and important physical properties of metals are density, melting point, specific heat, conductivity, thermal expansion; these properties decide the criteria for selection of material as bioimplant material.

Table 4. Materials used for making biomedical implants and devices.

Metals	Non-Metals		
Metals	**Polymers**	**Ceramics**	**Composites/matrix**
Stainless steel	Poly(methyl methacrylate)	Alumina	Epoxy
Titanium	Nylon 6/6	Zirconium	Polyacrylates
Chromium	Poly(ethylene terephthalate)	Pyrolytic carbon	Polymethacrylates
Nickel	Poly(lactic acid)	Bioglass-ceramics	Polyesters
Magnesium	Polytetrafluoroethylene	Calcium phosphates	Silicones
cobalt	Ultra-high-molecular-weight polyethylene		

Metals provide good yield strength, ductility stiffness and other excellent strength to the bioimplant material. Metals have been so successful because of their chemical structure of metals, as metals have positively charged ions surrounded by closed bound electrons. The positive ions form the hexagonal crystalline structure. The strong intermolecular bonding in metals occur due the strong ionic, covalent or metallic bonds and the weaker bonding occur due to the van dar Waals and hydrogen bonds, the interatomic bonding and the shifting of electrons leads to plastic deformation or permanent deformation as well as thermal and electrical conductivity of the metals. Metals are generally applied to places where load is an important factor and require rigidness such as hip joint, knee prostheses, and fracture fixation. Diffusion rate of metals is an important design parameter which defines the structure and properties of metallic components during solidification as casting, grain growth at elevated temperatures during annealing, growth of second phase particle, precipitation, and bonding of films as coatings, recrystallization to achieve the desired properties of the metal or alloy. It was observed that amorphous structures show interesting properties such as high hardness and excellent corrosion resistance. The perfect corrosion resistance appears because of the absence of dislocations, and other lattice defects (vacancies) related to sites for initiation of corrosion reactions **[12]**.

It has been seen in past that Metals have played a great role in technological development and even today used for most of the applications. In 1990 their developed a good understating of metallurgy combined with surgical techniques, which resulted in first implant of total hip made of stainless steel stem. Bio materials application also depends on the way of processing as it determines microstructure and thus defines properties such as ductility, strength, corrosion resistance etc. **[13,14]**. The fabrication technique such as casting, forging, machining. The metals are being used in different parts such as in the fields of orthopedics, dentistry, cardiovascular and neurovascular implants (e.g. Aneurysm clips) for forming cardiovascular devices (e.g., vascular stents, artificial heart valves, blood conduits and other components of heart assist devices) [15]. There are different applications of metals as implants such as- platinum which as an electrical conductive material is used as electrodes for cardiac pacemaker's implant and defibrillators. Other uses are as orthopedic applications for fractured part and replace the defective joints. Metals show good tensile strength, good fatigue resistance, and good wear resistance.

While mechanical failure cannot be overlooked and is unacceptable for most engineered structures, particularly for surgical implants where failure results in patient pain and, in certain cases, may reach to death for example heart valve component fracture, or may lead to complicated and life threatening revision surgery [16]. Some of the major elements used for making bioimplant are discussed in the following paragraphs **[3,4]**.

(a) Stainless Steel

Stainless steels are the most commonly used metals in biomedical because of their low cost and good strength, they are used for making joint replacement components but with this they are corrosive in nature and are implanted for short time period. The stainless steel components are made by forging followed by re-annealing till the final shape is obtained. The major type of stainless steel used is 316L, according to ASTM it is named as F138/139 which contains 17 % chromium, 10 % nickel and some other impurities. The letter L defines low carbon which is nearly around 0.03 %. Some of the stainless steels used for orthopedic applications as per ASTM are F138, F1314, F1586, and F2229 **[6]**.

(b) *Titanium*

Titanium is the most widely used metal in the field of biomedical for fabrication of orthopedic and dental implants. Pure Titanium has body-centered cubic (β-phase) at temperatures nearly 883°C and hexagonal close-packed structure (α-phase) at lower temperatures. It is used in two forms one pure and other as titanium alloy. It is lighter than stainless steel and has density half to that of stainless steel but shows same yield strength as stainless steel and are strong and its elastic modulus is half of that to stainless steel. the most common causes of failure of joints prostheses is aseptic loosening or failure due to improper plant which becomes unstable and affect the body other than disease **[18]**. In ideal situation the bone needs mechanical loading to maintain its structure and remodel effectively, but when the implant is done the whole load is absorbed by the implant which results in resorbing of the bone which leads to loosening of implant and further to failure, titanium its alloys show poor wear resistance. The pure titanium used is known by the name commercial pure titanium (cp titanium). It consists of 99 % of titanium and less than 1 % in the form of interstitial elements such as carbon, oxygen and nitrogen. Pure titanium forms single phase which makes it more ductile than its alloy Ti-6Al-4V and increases its formability.

Table 5. Classification of titanium alloys as per ASTM with applications.

ASTM Groups	Applications
GROUP I	Highest purity (lowest strength than, best room temperature ductility)
GROUP II	Mostly used for industrial dental implant
GROUP III	Small amount of iron is present in form of impurity.
GROUP IV	Shows highest strength than other grades, lowest ductility.

Fig. 4. Shows commercial dental implant designs **[4]**.

Pure titanium has been classified into four groups as per ASTM for different orthopedic applications **[17]**. It is also used for fracture fixation of bones. It is very expensive which reduces its use. It is used for permanent fixation as because of its non corrosive behavior and good strength. **Fig. 4** shows the use of pure titanium for dentistry use. It was seen that Osseo integrated end osseous dental implants were made in different shapes, which includes needles, hollow baskets, truncated cones blades, tripods, screws, cylinders, and disks. commonly used dental implant have a screw shape and is made up of commercial Ti or Ti-6Al-4V, as it is shown in **Fig. 4.** The dental implants are available with different diameters ranging from 3.3 mm to 6.0 mm and in lengths from 6 mm to 16 mm. Ti-6Al-4V ELI is the titanium alloys which consist of 6 % aluminum followed by 4% vanadium, ELI defines extra low interstitials which means very less impurities such as oxygen and carbon. Its ductility is more than pure titanium and strength is less, with high fracture toughness to make it more resistant to fatigue fractures, however, it has been observed that aluminum and vanadium shows toxic behavior with the body if remains for long time in the body. Titanium alloys are used for places where high strength is required such as hip and knee joints **[4]**.

(c) Cobalt and chromium alloys

The mixture of cobalt and chromium (Co-Cr) forms another alloying element used in the field of biomedical. These alloys are formed by forging and casting processes. It consists of approximately 56-70% cobalt and 22-30% chromium and small amount of other alloying elements. The most common Co-Cr alloy is Co-Cr-Mo consisting of 6% molybdenum other than cobalt and chromium. Some of the cobalt chromium alloys as defined by ASTM are as F75, F799 (low carbon), F799 (high carbon), F562, F563, F90 **[17]**. Other metals which are used for making alloys of cobalt and chromium are tungsten, nickel and iron. These alloys have higher corrosion resisting property and can be used form implant which has to be present in body for very long time. With this they have high strength, good fatigue resistance and are applied at the position where high loading is required such as total hip and knee joint replacement. They are hard and more resistant to wear, than titanium. These alloys are specially preferred where there is regular movement of body parts. They are expensive difficult to machine, and to fabricate **[4]**.

(d) Magnesium and their alloys

Owing to their high strength, ductility, and the property of good corrosion resistance, metallic materials like titanium, stainless steel, cobalt-based alloys, represents an important class of materials for hard tissue replacement. These materials are used in different load-bearing conditions by the implants for the repair and replacement of diseased and damaged tissues. These metallic materials are essentially seen neutral in vivo and remain inside the body after the implantation as temporary or permanent fixtures, which are removed from the body by a secondary surgical procedure after the complete healing of the tissue takes place sufficiently **[19]**. This additional surgery increases the costs of the health care system and can causes additional stress to patient. Thus, a new domain of research for researchers is in metallic implants which focus on biodegradable implants which can be dissolved in the biological environment after a certain time period of functional use. Magnesium can and provides both suitable mechanical properties and biocompatibility as a biodegradable material. Magnesium is present in our human body in large amounts. These ions help and are involved in many various metabolic reactions and different biological mechanisms; excess of magnesium is easily drained via urine **[20]**. When magnesium is compared to presently used implant materials, mg and its alloys have shown a lower elastic modulus of nearly 45 GPA and higher yield strength, which is closely found near to that of the natural human bone (10–40 GPa). These characteristics make magnesium-based alloys having the potential to reduce or avoid stress-shielding effects **[21-23]**. Magnesium and its alloys are applied and used as load bearing, lightweight, biodegradable, orthopedic implants which would maintain the mechanical integrity and remain in the body over the time scale, eventually being replaced by natural tissue **[24,25]**.

Magnesium is a white silvery material which is weak in its pure form and is mixed with other elements to make it strong enough to perform the desired task called magnesium alloys and are considered as the light weight material which have characteristics same as the natural bone and extremely biodegradable and biocompatible **[26-29]**. Magnesium is becoming a promising material because of its excellent mechanical and physical properties **[30]**. The density of magnesium is 1.73 g/cm^{3}at temperature of 20^{o}C which is slightly less than the natural bone of 1.8g/cm^3 **[31-33]**. Since, properties like density, mechanical property and nearby same elastic modulus as bone, magnesium and its alloys can solve the problem of stress shielding **[39]** and prevent bone resorption with proving itself as the promising material for development of biodegradable orthopedic implant materials **[34, 35]**. Magnesium alloys helps to enhance bone growth which is an excellent property as compared to other implant materials like titanium, titanium alloys, chromium cobalt alloys and stainless steels **[36, 37]**. In the past years, Magnesium based biometallic glasses, have emerged as excellent for bio-medical applications **[35, 38, 40]**. They are in single phase, which forms a chemically homogenous system with the absence of microstructural defects such as dislocations, grain boundaries, and precipitates **[41,42]**. This unique embodiment of random structure enables to have a high elastic limit which is combined with good corrosion resistance and high yield strength as compared to the crystalline equivalents **[42,43]**. However, there are some challenges that prevent the practical use of magnesium alloys as a biodegradable material. It can be seen that the commercial pure magnesium **[44]** and its alloys can get corroded very quickly at physiological (7.4–7.6) pH level and in the high conditions of chloride and the physiological environment. Rapid corrosion produces hydrogen gas during the corrosion process at a very fast rate which is very difficult to handle by the host tissue. This type of corrosion leads to the loosening of mechanical integrity of the tissue before it can heal fully **[45-47]**. To solve these problem properties of much higher inherent strength is needed to be developed in the alloys as their strength can deteriorate gradually during the degradation process **[48]**. It was reported that the Mg-Zn alloy decreased bending strength of the alloy during the starting corrosion stage; it observed that it decreased from 625 MPa to 390 MPa which was nearly 6% loss of weight.

It was seen in the study that human body contains about 99 % body magnesium is found in bone, muscles and other non-muscular soft tissue **[49]** 50–60 % of magnesium rests as surface substituent's of the total hydroxyapatite mineral component of the bone **[50]**, which is shown in **Fig. 5** **[51]**. Remaining of the magnesium is found in skeletal muscle and various soft tissues. The content of magnesium in bone decreases with the age, and magnesium stored in this form is not completely bio available during magnesium reduction **[52]**. Magnesium excretion is maintained by the different organs such as intestine, the bone and the kidneys. Mg is just like calcium which is absorbed by the gut and is stored in bone mineral, where as excess of magnesium is excreted through the kidneys and is moved out. Magnesium is absorbed by the small intestine by a passive Para cellular mechanism **[53,54]**, and some small amount is also taken by the large intestine **[55]**.

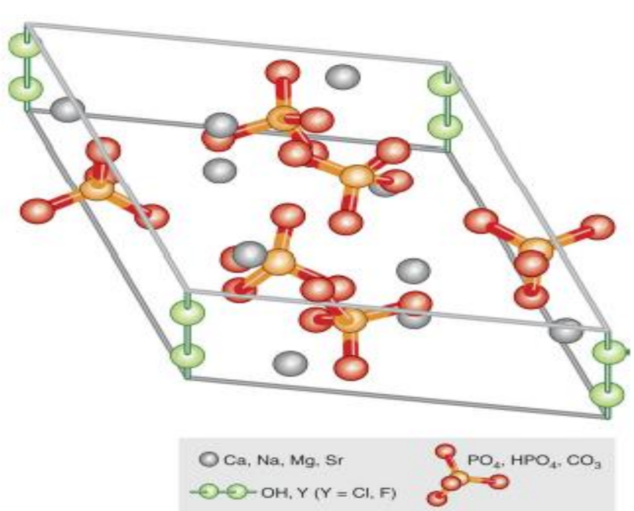

Fig. 5. Magnesium rests as surface substituents of the total hydroxyapatite mineral component of the bone **[51]**.

Hence the bone provides a huge exchangeable pool to buffer small changes in the serum magnesium concentration in body **[56]**. Overall, 1/3 of the skeletal magnesium is exchangeable, which serves as a reservoir for managing physiological extracellular magnesium level content **[56]**. It ranges from 5 to 20 mmol/L and 1 to 5 % is ionized; the remaining is bound to proteins contents and adenosine triphosphate **[53]**. Extracellular magnesium is primarily found in serum and red blood cells which accounts for ~1% of total body magnesium **[53,57,51]**.

Despite of all these desirable properties of magnesium and its alloys for different medical bio implants and other medical applications, the fast degradation of magnesium is a critical challenge in vivo test [58]. Many factors affect the degradation of magnesium, such as microstructure, bulk composition, and composition at the surface of the magnesium alloy, with composition of the surrounding fluids. It becomes an important factor to understand the interactions between all these Sources and recognize the role of every individual factor on degradation of magnesium. One method of the magnesium degradation controlling is to insert certain elements for alloying to the magnesium. Yttrium (Y) is being often added to mg alloys to increase their material strength **[59,60]**, ductility **[61]**, and corrosion resistance **[62,63]**. However, Y exhibits degradation inhibiting and degradation promoting both activities in mg alloys, keeping in mind other factors **[64]**. Yttrium oxide accumulates in the form of degradation layer, which migrates Y to the metal surface and is oxidized **[65,66,67]**. Stable degradation layer slows down the degradation of magnesium by inhibiting cathodic reactions **[67]**. When certain alloy improves corrosion resistance in one environment it is possible that it may accelerate the degradation in some other environment. Therefore, it becomes important to elucidate interaction of the factors influencing mg alloy degradation to tailor the magnesium alloy more effectively for different intended applications at various locations in vivo, thus desirable life span for magnesium based biodegradable implants and its alloys can be achieved. Composition of material is considered as crucial factor as observed in the study that most of the material available commercially are toxic to the human body. Therefore, it becomes important to choose suitable material which has the desired mechanical properties and is biocompatible with body.

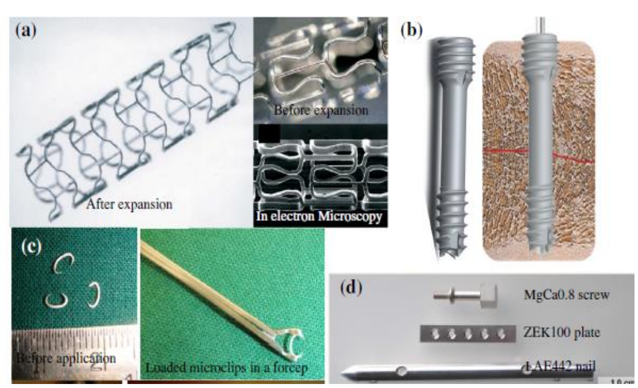

Fig. 6. Different biodegradable magnesium parts **[75].**

Table 6. Shows categorization of magnesium groups with its alloying elements.

Categories	Alloying element	Alloys
Group 1	Pure magnesium	Mg
Group 2	Al and RE as an alloying elements	AZ91, AZ31 AE21
Group 3	Without Al alloys	Mg-Ca, WE, MZ WZ

Some of the minerals such as calcium, magnesium, zinc and others which are shown in **Table 6 [68-73]** are used for alloying magnesium to form its alloys these minerals are also used by body for growth can play a better role as biodegradable material which is biocompatible and non toxic. With this entire factor the material should have controllable degradation rate and dissolution rate that permits the mechanical integrity and maintains the rate of healing till the infected part get fully recovered, and proper absorption or excretion of the degraded material **[74]**.

Table 7. Classification of improving strength of bioimplant.

1.	Proper selection of material.
2.	Grain structure refinement.
3.	Corrosion resistant techniques.
4.	Formation of inter-metallic phases.
5.	Composites.

Magnesium and its alloys are grouped in 3 categories which are shown in **Table 6**. The physical and mechanical properties of the magnesium and its alloys can be improved by different processes which are briefed in **Table 7**.

Table 8. Element and their effect on body.

Element	Mechanical property	Effect
Al	Improves corrosion resistance, increases strength	Accumulates in bone tissue/decreases osteclast viability
Ca	Improves corrosion resistance	Leads to formation of excess calcium in the kidneys (stones).
Cu	increase strength	produce cellular cytotoxicity
Mn	improve corrosion resistance	produces neurological disorder
Li	Improves corrosion resistance	Overdose causes central nervous center disorders and lung dysfunctions
Zn	Improves yield stress, Reduce hydrogen gas evolution during bio-corrosion.	Hinders the bone development.
RE	Improvement in corrosion resistance	Accumulate in the liver and bone

Table 9. Application of bioimplant material and in different fields.

Implant Materials	Function and applications
Stainless steel	Joint replacements (hip, knee), Bone plate for fracture fixation, Dental implant for tooth fixation, Heart valve, Spinal Instruments, Surgical Instruments, Screws, dental root Implant, pacer, fracture plates, hip nails, Shoulder prosthesis
Titanium and its Alloys	Cochlear replacement, Bone and Joint Replacements (hip, knee), Dental Implants for tooth fixation, Screws, Suture, parts for orthodontic surgery, bone fixation devices like nails, screws and plates, artificial heart valves and surgical instruments, heart pacemakers, artificial heart valves
Cobalt-chromium alloy	Bone plate for fracture fixation, Screws, dental root implant, pacer, and Suture, dentistry, orthopedic prosthesis, Mini plates, Surgical tools, Bone and Joint replacements (hip, knee), dental implants
Magnesium and its alloys	Stents, dentistry, orthopedic prosthesis, Mini plates,

Weakness of the biomedical implant material

With all these advantages of magnesium and its alloys there are some weaknesses which are to be looked and very much important to study for proper functioning and bio compatibility with the human body fluid. Some of the major are explained with their importance.

Fracture

It was observed that if there exist a large difference in elastic constants of the metals (stainless steel, Co-based alloys, Ti and its alloys). Some time they are commonly used for forming bone-interfacing implants for different orthopedic applications can lead to undesirable structural changes in the bone and other parts which are situated next to a metallic implant in different conditions. Where the implants are fastened to bone for joint replacement and fracture stabilization and orientation in the length of the implant juxtaposing a significant length of bone such as a host femur's changed by femoral hip implant stem component. The reinforced composite formed by the bone and the metal component should bear the major stresses. However, the high modulus variation in bone and implant material leads to stress shielding because of which high stresses are generated in the bone where the force is transferred from metal to the bone and can cause defect **[3,4]**.

Corrosion

One of the major problems which can be observed during the implant of metal in biomedical environment is corrosion. Some metals such as Mg, Ti, Co, Cr, Ni, and Pt are able to resist the corrosion up to an acceptable degree while working in the worse environment. These metals rely on formation of oxide layer on the base metal which stops them in getting direct contact with the outside environment **[76]**. It depends on the metal composition and the surrounding environment. It was also observed in the study that corrosion can be reduced to a large extent by proper selection of material and proper characterization of the host site **[77]**. Metals have been so successful because of their chemical structure of metals, as metals have positively charged ions surrounded by closed bound electrons. The positive ions form the hexagonal crystalline structure. The strong intermolecular bonding in metals occur due the strong ionic, covalent or metallic bonds and the weaker bonding occur due to the van-deer Waals forces and hydrogen bonds, the interatomic bonding and the shifting of electrons leads to plastic deformation or permanent deformation as well as thermal and electrical conductivity of the metals. Metals are generally applied to places where load is an important factor and require rigidness such as hip joint, knee prostheses, and fracture fixation. Diffusion rate of metals is an important design parameter which defines the structure and properties of metallic components during solidification as casting, grain growth at elevated temperatures during annealing, growth of second phase particle, precipitation, and bonding of films as coatings, recrystallization to achieve the desired properties of the metal or alloy. It was observed that amorphous structures show interesting properties such as high hardness and excellent corrosion resistance. The perfect corrosion resistance appears because of the absence of dislocations, and other lattice defects (vacancies) related to sites for initiation of corrosion reactions **[12]**.

It has been seen in past that Metals have played a great role in technological development and even today used for most of the applications. In 1990 their developed a good understating of metallurgy combined with surgical techniques, which resulted in first implant of total hip made of stainless stem. Bio materials application also depends on the way of processing as it determines microstructure and thus defines properties such as ductility, strength, corrosion resistance **[13,14]** the fabrication technique such as casting, forging, machining. The metals are being used in different parts such as in the fields of orthopedics, dentistry and neurovascular implants (e.g. Aneurysm clips) for forming cardiovascular devices (e.g. vascular stents, artificial heart valves, blood conduits and other components of heart assist devices) **[3]**. There are different applications of metals as implants such as-platinum which is an electrical conductive material is used as electrodes cardiac pacemakers implant and defibrillators. And other uses are as orthopedic applications for fractured part and replace the defective joints. Metals show good tensile strength, good fatigue resistance, and good wear resistance. While mechanical failure cannot be overlooked and is unacceptable for most engineered structures, particularly for surgical implants where failure results in patient pain and, in certain cases, may reach to death for example heart valve component fracture, or may lead to complicated and life threatening revision surgery **[4,16].**

Conclusion and future perspectives

Magnesium chemistry is unique among cations for biological relevance. Magnesium is necessary for humans and is required in good amounts. Magnesium is a cofactor in more than 300 enzymatic reactions and very much essential for many different physiological functions, like vascular tone, muscle contraction and relaxation, maintaining heart rhythm, and nerve function. Magnesium is also very much needed for the formation of bone and is referred as natural 'calcium antagonist'. In past few years, significant advancement has been done in the field of biodegradable and bioabsorbable materials and magnesium have shown a great potential as a material for bioimplant, further a lot of research is needed to evaluate the potential of Magnesium-based alloys for different uses in human biological implants. An integrated approach involving material scientists, medical professionals, chemists, experimental and computational material scientists, is needed to understand and describe the fundamental mechanisms which is involved in the application of magnesium alloys in various physiological conditions. Understanding the various fundamental questions such as the degradation rate, corrosion surface interaction with tissue, degradation products influence on the surroundings, and toxicity aroused by different alloying elements is necessary to be achieved for a biocompatible magnesium and biodegradable Magnesium alloy implant. The usage of magnesium as biodegradable alloys faces some challenge like that their corrosion/degradation rates under various physiological environment. One of the useful methods to reduce down corrosion rate of magnesium alloys is surface modification, using electrode position, alkaline heat treatment, phosphate treatment, microarc oxidation.

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