Biodegradable Stent to Prevent Restenosis in Coronary Artery Lesions

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***Abstract*:- Damage and disease in the heart arises the need for developing biomedical implants. Magnesium and its alloys have been intensively studied as biodegradable implant materials, where their mechanical properties make them a potential candidate for many applications. As a biocompatible and biodegradable metal, it has several gains over the metallic implants presently in use, including eliminating the effects of stress shielding, improving (Fe). Bioactivity and degradation studies are evaluated by immersing the samples in simulated body fluid (SBF) for a certain period of biocompatibility concerns in vivo and eliminating the requirement of a second surgery. In this project work magnesium (Mg) is fused with ferrous(Fe) and it was coated with polymer. The bioactivity and degradation studies were assessed by determining the rate of corrosion by weight loss method, polarisation studies and Ac impedance measurements.**

Keywords: Magnesium, Ferrous, bioactivity, simulated body fluid (SBF)

1. INTRODUCTION

Annually several million people suffer by various cardiac diseases. Many of cardiac diseases are too complex for an external medical treatment but have to be surgically fixated by internal biomaterial implants. Traditional methods use permanent metal implants have to be excised. Especially young patients in growth require the implant removal. Usually, metal implants should be removed latest one or two years after the first surgery. Biodegradable implants, which dissolve in the human organism, therefore represent an appropriate solution. Clinical circumstances often require the application of implants that serve temporarily rather than for a permanent purpose (Table 1.1). In these circumstances degradable biomaterials are of interest because the implants fabricated from these materials do not need to be surgically removed. The surgical removal of an implant with a temporary purpose is undesirable, as the process creates another wound with the possibility of surgical complication and infection. Additionally, the use of degradable implants can sometimes sidestep problems related to the long-term safety of permanent implants, such as long-term immune rejection, chronic inflammation at the implant–tissue interface, and failure of the implant. However, degradable implants are not without their own safety concerns, such as the toxicity of their degradation products, and the degradation-related, early failure of the implant. Therefore, designing a degradable implant requires careful testing for potential toxicity of its degradation products and careful consideration of the implant's mechanical integrity during the required service life of the implant. This project work is analysis of biodegradable metal(Mg and Fe) with polymer coating. The analysis is based on cardiac stent metal. Before knowing about this analysis, the basic information about the heart, heart blocks and the types have been discussed.

Table 1.1 Medical application of degradable biomaterials

Applications	Comments
Sutures	The earliest successful application of Degradable biomaterial in human body.
Orthopedic fixation devices	Requires material of exceptionally strength and stiffness
Temporary vascular grafts and stents made of degradable material	Only investigational devices are presently Available

2. EXISTING SYSTEM

Coronary artery disease (CAD) is the leading cause of morbidity and
mortality in the world. Central to the pathogenesis of CAD is the development
of atherosclerotic lesions in coronary arteries. These lesions, if unstable or clinically significant, are frequently treated with percutaneous coronary intervention (PCI), which usually involves balloon angioplasty and stent implantation. PCI is one of the commonest procedures performed in contemporary clinical practice, with more than 1400 procedures/million carried out every year in the UK. The coronary stents have substantially evolved since their first use in 1980s and there are on-going studies to refine their design, structure and material.

2.1 History of coronary stents

Since the introduction of percutaneous transluminal coronary angioplasty (PTCA) by Gruntzig in 1977, major advancements have been made in the clinical practice of percutaneous coronary intervention (PCI). Puel and Sigwart, in 1986, deployed the first coronary stent to act as a scaffold, thus 1) preventing vessel closure during PTCA, and 2) reducing the incidence of angiographic restenosis, which had an occurrence rate of 30-40%.[1] By 1999, stenting composed 84.2% of all PCIs.Despite the widespread use of these devices, bare metal stents (BMS) have been associated with a 20-30% restenosis rate requiring reintervention. Restenosis occurs as a result of neointimal hyperplasia—growth of scar tissue within the stent—due to the proliferation and migration of vascular smooth muscle cells. This phenomenon is clinically evident within the first 6-9 months after stent placement, and occurs in response to strut-associated injury and inflammation. In addition to restenosis, PTCA and BMS implantation cause exaggerated endothelial injury and inflammation, rendering both the stent and vessel highly thrombogenic. A fibrinogen layer covers the stent surface, further inducing platelet activation and thrombosis. Adjunctive anti-platelet medication is crucial in preventing local coronary thrombosis, myocardial infarction (MI), and death.Current recommendations for patients with BMS include dual anti-platelet therapy with aspirin and clopidogrel, which are continued for 6 weeks to allow complete endothelialization of BMS. Wilson et al. in 2002 reported similar findings in patients who underwent noncardiac surgery. The incidence of MI and death were significantly lower among patients who underwent surgery after their 6-week course of aspirin and clopidogrel were completed.

In 2001, drug-eluting stents (DES) were introduced as a strategy to minimize restenosis and requirement for reintervention. The currently available polymer-coated stents contain antiproliferative agents which elute locally in the implanted coronary artery to prevent neointimal hyperplasia. Initial animal studies demonstrated a clear benefit over BMS (4-6% restenosis versus 20-30%), and early clinical trials further supported this. In addition, at 2-year follow-up using both angiography and ultrasound, the clinical safety of DES was further established with minimal late lumen loss observed. A recent pooled analysis demonstrated a 74% reduction in the risk of target lesion revascularization for both sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) compared to BMS.At present, 90% of all stents placed in the United States and Europe are DES.Despite the enthusiasm that resulted with the advent of DES, incomplete endothelialization and stent thrombosis continue to plague these devices. Initial animal studies demonstrated complete endothelialization with BMS at 28 days, whereas DES uniformly showed incomplete healing at 180 days.Based on early observations in both animal and human studies, it was recommended that patients with DES receive dual anti-platelet therapy with aspirin and clopidogrel for at least 3-12 months, followed by life-long aspirin therapy, depending on the stent placed and the pre-existing comorbidities which further increase the risk of stent thrombosis Despite this regimen, late stent thrombosis (LST)—defined as occurring >30 days post-stent insertion—remains a significant complication in patients with DES. Late stent thrombosis carries a 45% mortality rate. It presents as an ST-segment elevation myocardial infarction (STEMI) or sudden death. Late stent thrombosis has been documented in both clinical and autopsy studies in patients as far as 4 years after stent insertion.Further, LST is associated with the 1) discontinuation of clopidogrel +/- aspirin, 2) stable aspirin monotherapy, or 3) a hypersensitivity reaction to the stent polymer, or to the antiproliferative agent (sirolimus vs. paclitaxel).A recently published study reported that patients with DES implanted had significantly increased rates of death when clopidogrel was discontinued at 6-, 12-, and 24-months when compared to patients who remained on this therapy at the same time intervals.

3. PROPOSED SYSTEM

3.1. MATERIALS AND METHODS

3.1.1. Magnesium

The lightest structural material (1.8g/cm3), magnesium is the 8th most abundant element in the earth's crust. It occurs naturally in Dolomite, Magnesite, Carnallite and Chloride (sea water)

- Lightest of all structural materials
- 75% lighter than steel
- 33% lighter than aluminum
- High impact resistance
- High strength to weight ratio
- Can be cast to net shape
- Excellent dimensional stability/repeatability
- 100% recyclable

3.1.2. Role of magnesium in body

Magnesium is needed for more than 300 biochemical reactions in the Body. It helps to maintain normal nerve and muscle function, supports a healthy immune system, keeps the heart beat steady, helps bone remaining strong. It also helps in production of energy and protein.

Enzyme activity , enabling thousands of bio-chemical processesEnergy production and ATP, the energy storage unit of the body’s cellsDNA and RNA , the body’s internal instructions for building proteins and new cellsMineral balance , necessary to maintain cell life

3.1.3. Iron

t Iron is a chemical element with symbol Fe It is a metal in the first transition series. It is by mass the most common element on Earth , forming much of Earth's outer and inner core . It is the fourth most common element in the Earth's crust. Its abundance in rocky planets like Earth is due to its abundant production by fusion in high-mass stars

3.1.4. Role of iron in body

Iron plays an important role in biology , forming complexes with molecular oxygen inhemoglobin and myoglobin ; these two compounds are common oxygen transport proteins in vertebrates. Iron is also the metal at the active site of many important redoxenzymes dealing with cellular respiration andoxidation and reduction in plants and animals. A human male of average height has about 4 grams of iron in his body, a female about 3.5 grams. These 3-4 grams are distributed throughout the body in hemoglobin, tissues, muscles, bone marrow, blood proteins, enzymes, ferritin , hemosiderin , and transport in plasma.

3.1.5. Simulated body fluid (SBF)

Simulated body fluid that has inorganic ion concentrations similar to those of human extracellular fluid, in order to reproduce formation of apatite on bioactive materials invitro . This fluid can be used for not only evaluation of bioactivity of artificial materials invitro , but also coating of apatite on various materials under biomimetic conditions.

The pH of SBF is adjusted to pH 7.25 at 36.5 ° C, by using 50 mM(mol/dm^3) of tris(hydroxymethyl)aminomethane and approximately 45 mM of HCl. When apatite-forming ability of the specimen is not so high, pH of SBF is sometimes adjusted to pH 7.40.

3.1.6. Preparation of sample

Pure magnesium is relatively unstable and does not occur in nature in metallic form. When strongly heated in air it oxidizes violently so as to burn with a brilliant bright light, which ac counts for its use in pyrotechnics.

However, prior to this application it has not been considered practicable or possible to alloy magnesium with iron or steel, probably because of its low melting point (1202 F.) and its tendency to burn violently at temperatures at or above 1000 F. Hence, if pure magnesium is introduced into molten iron or steel, or is associated with iron or steel at higher temperatures, it reacts violently or explodes and volatilizes instead of combining with the ferrous metal.

The process of alloying magnesium with ferrous metal, which consists in covering pure magnesium with fire clay and heating to melt the magnesium, cooling and separating the resulting magnesium mass and pulverizing the same, mixing the said pulverized mass with a small amount of said fire clay, and then adding said mixture to the ferrous metal in a highly heated condition.

The process of alloying magnesium with ferrous metal, which consists in covering pure magnesium with fire clay having an approximate analysis of 57.22% silica, 25.19% alumina, 5.59% ferrous oxide, .70% calcium oxide and 1.86% a ne um ide h tin he ch r e to m l h magnesium, cooling and separating the resulting magnesium mass from the clay and pulverizing the mass, mixing said pulverized mass with a small amount of said fire clay, and then adding said mixture to the ferrous metal in a highly heated condition.

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The process of alloying magnesium .with ferrous metal, which consists in covering pure magnesium with fire clay in the proportions of about four to five parts by volume of clay to one part of magnesium, heating said covered magnesium to melt the same, cooling and separating the solidified magnesium mass from the clay, pulverizing said solidified magnesium mass and mixing it with one to two per cent by volume of, said fire clay, and then adding said mixture to molten ferrous metal.

3.1.7. Polymer

A **polymer** (/ˈpɒlɪmər/; Greek *poly-*, "many" + *-mer*, "part") is a large molecule, or macromolecule, composed of many repeated subunits. Due to their broad range of properties, both synthetic and natural polymers play essential and ubiquitous roles in everyday life. Polymers range from familiar synthetic plastics such as polystyrene to natural biopolymers such as DNA and proteins that are fundamental to biological structure and function. Polymers, both natural and synthetic, are created via polymerization of many small molecules, known as monomers. Their consequently large molecular mass relative to small molecule compounds produces unique physical properties.

3.1.7.1.CHITOSAN

Other names

Poliglusam; Deacetylchitin; Poly-(D)glucosamine; BC; Chitopearl; Chitopharm; Flonac; Kytex

Related compounds

D-glucosamine and
N-acetylglucosamine (monomers)

Chitosan is a linear polysaccharide composed of randomly distributed β-(1→4)-linked D-glucosamine(deacetylated unit) and *N*-acetyl-D-glucosamine (acetylated unit). It is made by treating the chitin shells of shrimp and other crustaceans with an alkaline substance, like sodium hydroxide.

Chitosan has a number of commercial and possible biomedical uses. It can be used in medicine, it is useful in bandages to reduce bleeding and as an antibacterial agent; it can also be used to help deliver drugs through the skin.

More controversially, chitosan has been asserted to have use in limiting fat absorption, which would make it useful for dieting.Other uses of chitosan that have been researched include use as a soluble dietary fiber.

3.1.7.2. Polycaprolactone

Polycaprolactone is a biodegradable polyester with a low melting point of around 60 °C and a glass transition temperature of about −60 °C. The most common use of polycaprolactone is in the production of speciality polyurethanes.

Density: 1.145 g/cm³
Melting point: 60 °C (140 °F)
Chemical formula: $(C_6H_{10}O_2)_n$
Abbreviations: PCL

Other names
2-Oxepanonehomopolymer
6-Caprolactone polymer

Polycaprolactone (**PCL**) is a biodegradable polyester with a low melting point of around 60 °C and a glass transition temperature of about −60 °C. The most common use of polycaprolactone is in the production of speciality polyurethanes. Polycaprolactones impart good resistance to water, oil, solvent and chlorine to the polyurethane produced. This polymer is often used as an additive for resins to improve their processing characteristics and their end use properties.

4.EXPERIMENTS

4.1. Weight loss method

Weighed metal coupons are put in the corrodant solution for known period of time and the amount of metal going into solution is determined to evaluate the corrosion rate.

4.2. Potentiodynamic Polarization method

The corrosion process is regarded as an electrochemical phenomenon consisting of anodic (metal dissolution) and cathodic processes. [19] Hence the behaviour of the inhibitor can be understood by carrying out separately cathodic and anodic polarizations in the presence and absence of inhibitor. The corrosion current can be measured by extrapolating the anodic and cathodic polarization curves to the value of corrosion potential.

When a metal is not in equilibrium with a solution of its ions, the electrode potential differs from the free corrosion potential by an amount known as the polarization (η). Other terms having equivalent meanings are overvoltage and over potential. Polarization is an extremely important corrosion parameter which enables useful statements to be made about the rates of corrosion processes.

The model generally used for the corrosion process assumes that the rates of both the anodic and cathodic processes are controlled by the kinetics of the electron transfer reaction at the metal surface. An electrochemical reaction under kinetic control obeys the simplified Tafel Equation

$$\mathbf{E = a + b \log I}$$

where, E is the electrode potential of the specimen

I is the current resulting from the reaction
a and b are constants

The Tafel equation describes the behaviour of an isolated reaction. In a corrosion system, there are two opposing reactions – anodic and cathodic. The Tafel equations for both the anodic and cathodic reactions in a corrosion system are derived from the Butler-Volmer Equation.

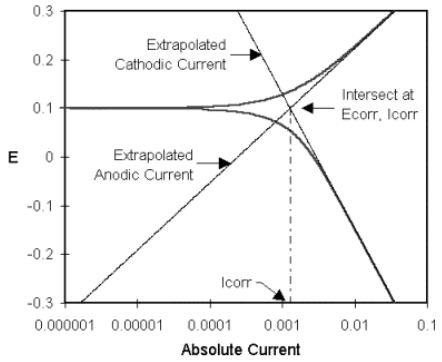

Fig. 4.1 A Typical Tafel plot

A classic Tafel analysis is performed by extrapolating the linear portions of a log current versus potential plot back to their intersection**.** The value of either the anodic or the cathodic current at the intersection is I_{corr}.

5.CONCLUSION

The corrosion of Mg/Fe alloy in 1N SBF solutions after different exposure intervals have been investigated using potentiodynamic polarization (CPP), and impedance spectroscopy (EIS) measurements. The study was complemented by weight-loss data after exposure periods varied 6 days.

Electrochemical measurements indicated that the dissolution of Mg/Fe alloy decreased with increasing the immersion time from 0 min to 60 min and also decreased the uniform corrosion, while increase the pitting attack for the alloy. Gravimetric (weight loss) measurements confirmed the uniform corrosion of the alloy and its rate increases with the increase of its exposure time. It also confirmed that the immersion time decreases the uniform corrosion of Mg.