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ZINC, MAGNESIUM AND TANTALUM FOR BIOMEDICAL APPLICATIONS: A COMPREHENSIVE REVIEW

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ABSTRACT

The historical development and biomedical applications of magnesium, tantalum, and zinc are examined in this integrated study. It traces the development of magnesium from its use in military applications through its integration into many businesses, with an emphasis on its use in orthopaedic implants. Along with early attempts and failures in orthopaedic implantation, the mechanical properties of magnesium alloys suitable for biodegradable osteosynthetic materials are investigated. Clinical cases highlighting the successes and difficulties of magnesium implants in bone restoration are presented. Magnesium alloys have recently played important roles in biomedicine, particularly in stents and scaffolds. This analysis highlights their biocompatibility and corrosion behaviour. The numerous biomedical applications of tantalum and zinc, such as those in implants, surgical equipment, and drug delivery, are then discussed. Tantalum's porosity, biocompatibility, and biomechanical qualities make it the ideal material for implants, producing positive results in bone, tissue, and dental applications. Zinc's robust antibacterial characteristics and promise in targeted drug release are highlighted. Innovative manufacturing techniques, composite optimisation, surface alterations, and thorough clinical assessments are among the future directions. Key areas of interest include standardised testing, tissue interactions, and regulatory frameworks. This paper highlights the crucial contributions of tantalum, magnesium, and zinc to the development of biomedical engineering and provides insights for improved patient care, innovation, and therapeutic efficacy.

Keywords: Zinc, magnesium, tantalum, biomedical applications, implants, alloys.

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1. INTRODUCTION

In orthopaedic procedures, zinc-coated implants were developed to encourage the bone formation and lower the possibility of implant failure. The following described studies are part of the investigation of the use of zinc and its alloys for potential biomedical applications.

It has been noted that calcium phosphate minerals are crucial for bone regeneration and that zinc plays a function in bone metabolism. Adding zinc to calcium phosphate substances to improve their osteogenic qualities. putting the calcium phosphate implants that release zinc into rabbits' femora and watching them for 4, 8, and 12 weeks. In contrast to non-zinc-releasing implants, the zinc-releasing implants had a stimulatory impact, improved implant integration, and mechanical stability on bone development [1].

Magnesium-Manganese-Zinc (Mg-Mn-Zn) alloy benefits from biocompatibility and mechanical attributes. Analyzing samples of Mg-Mn-Zn alloy implanted into rabbit femurs for 1, 2, 4, 8, and 12 weeks. The corrosion behaviour of the Mg-Mn-Zn alloy was affected by the time of implantation, and the alloy exhibited good biocompatibility-no major tissue reaction was noticed- in the physiological environment. It also had a reasonably moderate corrosion rate [2].

Secondly, Tantalum is an atomic number 73 chemical element with the symbol Ta. Tantalum is a transition metal that is extremely hard, ductile, glossy, blue-gray, and has a strong corrosion resistance. It belongs to the family of metals known as refractory metals, which are frequently employed to make strong alloys with high melting points [3]. Along with vanadium and niobium, it is a group 5 element that is always found in geologic sources with niobium, which is chemically comparable to tantalite, columbite, and coltan.

Tantalum is a valuable material for laboratory and industrial equipment including reaction containers and vacuum furnaces because of its chemical inertness and extremely high melting temperature. Tantalum capacitors for electronic devices like computers use it. Its potential use as a component of superior superconducting resonators for quantum processors is being researched [3].

Thirdly, Magnesium has had a significant impact on civilization since its discovery. Early on, conflicts and military uses fueled its development. Magnesium, for instance, was weaponized to create incendiary bombs, flares, and ammunition that were later employed in World War II and resulted in enormous fires and extensive destruction. After the war, the availability and distinctive combination of qualities of magnesium were investigated and found to be extremely appealing for a wide variety of applications. Today, consumer electronics, aerospace, and the automobile industries all employ magnesium in technical applications. It also plays a part in organic chemistry and medicines and is employed in the production of several general-purpose items, including furniture, sporting goods, and office supplies [4].

1.1 Background of Study and Motivation

Due to its beneficial qualities, such as its capacity to encourage bone formation and its antimicrobial capabilities, zinc has been utilised in numerous applications for several years. Dental amalgam is frequently used as a restorative substance, although both researchers and the general public are concerned about its potential health dangers. Dental amalgam is made up of a combination of metals, including tin, copper, silver, and mercury. The most poisonous component of amalgam may have a negative impact on health. From 1990 to the present, several applications of zinc and its alloys have undergone development [5].

On the other hand, tantalum was found in Sweden in the year 1802. It was once believed that tantalum and columbium belonged to the same element. Heinrich Rose, a German chemist, challenged this finding in 1846, claiming that the tantalite sample included two extra elements [2]. Three scientists-Christian Blomstrand, Henri Sainte-Claire Deville, and Louis Troost- distinguished tantalum from niobium in 1864. Werner von Bolton created the first pure ductile metal at Charlottenburg in 1903. Up until tungsten superseded it, light bulb filament was made of metallic tantalum wires [6].

Furthermore, Magnesium is a lustrous, silvery-white metal that belongs to the family of alkaline earth metals. In nature, it is never found unbound and is abundant on Earth and in space but is also very reactive. Before Joseph Black (1754), with assistance from Friedrich Hoffman (1729), identified it as an element, it existed as a chemical compound. Antoine-Alexander Bussy produced the first pure magnesium in 1828 despite Humphry Davy discovering the first magnesium metal in 1808 [4].

The origins of sustainable magnesium implants started not long after Sir Humphrey Davy's discovery of elemental magnesium in 1808. By electrolyzing fused dried MgCl2, his colleague Michael Faraday discovered how to create Mg metal in 1833. The first person to realise that Mg could be manufactured economically by electrolysis was Robert Bunsen, who designed a modest laboratory cell for the hydrolysis of fused magnesium chloride in 1852. The 1862 London World's Fair included some authentic Mg products [7]. Most likely, three human patients' bleeding vessels were stopped by Edward C. In 1878, Huse used a few of those Magnesium strands as ligatures. He had already discovered that magnesium corroded more slowly in living creatures and that how long it took for the metal to entirely erode depended on the size of the Magnesium strand used. Huse expressed much enthusiasm in his writing on the metal's biodegradable qualities [7].

Many other doctors were inspired by the Graz-based Austrian surgeon Erwin Pair to use disposable magnesium implants more frequently in a variety of surgical procedures. He began his initial Mg resorption tests in 1892 [7], but his biggest challenge at the time was obtaining filigree-fabricated Mg devices for his research. They received pure Mg sheets, plates, pins, spheres, wires, pegs, cramps, and nails in 1898 [8]. Around 1900, Payr proposed that cell water and oxygen content, salt content in blood, carbon dioxide, and cell chemical processes were the main contributors to magnesium corrosion in vivo. Albin Lambotte was also a pioneer in the study of biodegradable magnesium. He also served as Jean Verbrugge's mentor and maintained and expanded clinical research and animal testing [8].

1.2 Need of Study

Conduct comparative studies to assess zinc, tantalum, and magnesium-based materials' biocompatibility, mechanical attributes, corrosion resistance, and tissue integration. Investigate biocompatibility in vitro and in vivo, on a long-term basis to understand potential hazards and benefits. Explore novel uses in implants, tissue scaffolds, drug-delivery systems, and biomedical devices. Improve biocompatibility, corrosion resistance, and functional qualities by studying surface modification techniques. Investigate antibacterial qualities and their potential for preventing and treating infections in biomedical implants and equipment.

Discover the development of biodegradable alloys of zinc, tantalum, and magnesium for transient implants and devices, ensuring safe and controlled degradation without harmful effects on the body. Conduct clinical investigations to evaluate the security, effectiveness, and long-term performance of materials in medicinal applications. Explore cutting-edge fabrication methods like additive manufacturing (3D printing) to create complex structures and unique designs. Establish standardized testing procedures, quality assurance procedures, and regulatory standards to ensure safe and efficient deployment. Study the biodegradation processes of zinc-based materials to understand their kinetics, corrosion behavior, and tissue responses. This information will help create better zinc-based biomaterials with tailored characteristics and controlled breakdown rates. Scientists and engineers can contribute to the development of novel and efficient biomedical solutions with enhanced biocompatibility, functionality, and clinical results by addressing these research needs.

2. MATERIALS AND METHODS

2.1 Classification of Materials by Applications

As shown in the figure-1, based on the biomedical applications Zinc, Tantalum, and Magnesium are further classified and their evolution is carried out:

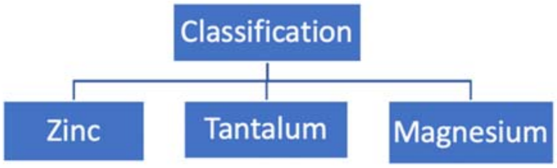

Figure-1. Bio-metals classification.

The metals are evaluated considering their historical, medieval, and modern uses. The journey of metals and their entry into the biomedical field is highlighted. Figures 2 and 3 highlight the biomedical applications of the specified metals but are not only restricted to a few applications.

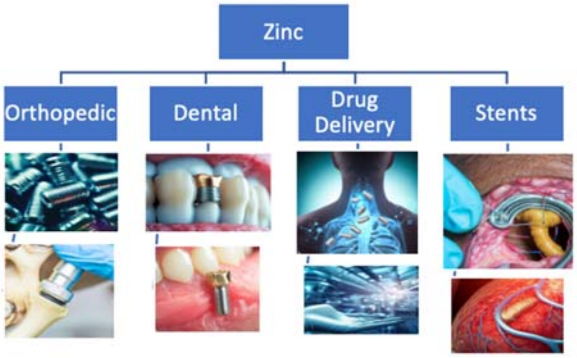

Figure-2. Zinc and its biomedical applications.

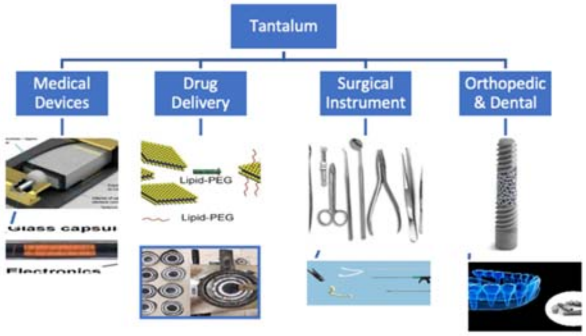

Figure-3. Tantalum and its biomedical applications.

2.2 List of Materials and Their Alloys

The elements alloyed in a desired percentage with the use of metal enhance the properties of the base metal. To achieve a desired property without any loss of the base property the alloying elements are used. The Table-1 shows the alloyed metals used for biomedical applications and their enhanced properties.

Table-1. Enhanced properties of Alloys.

S. No.	Alloy	Enhanced Properties
1	Mg - Mn - Zn	Biocompatibility, Corrosion resistance, Mechanical strength, Antibacterial properties, Biodegradability [9 - 12].
2	Mg - Ca - Zn	Biocompatibility, Resistance to corrosion, Mechanical strength, Osteogenic properties, Antibacterial properties, and Biodegradability [13 - 19].
3	Mg - Ca - Sr with Zn contents	Biocompatibility, Resistance to corrosion, Mechanical strength,
		Osteogenic properties, Antibacterial properties, and Biodegradability [13 - 19].
4	Silver and Zinc doped	Antibacterial properties, Biocompatibility, Resistance to corrosion [5, 20].
5	Mg - Zn - GO	Biocompatibility, Corrosion resistance, Mechanical strength, Antibacterial properties, Biodegradability [26 - 30].
6	Copper-zinc superoxide dismutase (CuZnSOD)	Antioxidant properties, Biocompatibility [33 - 36].
7	Au - Cu - Zn	Biocompatibility, Corrosion resistance [33 - 36].
8	Zinc Oxide-Eugenol (ZOE)	Antimicrobial properties, Biocompatibility [34, 35].
9	Au - Ag - Cu - Zn - Sn	Biocompatibility, Corrosion resistance [40 - 43].
10	Zinc Phthalocyanine (ZnPC)	Photodynamic Therapy Applications and Biocompatibility [44, 45].
11	Ni - Zn	Magnetic properties, Biocompatibility, and Corrosion resistance [46 - 48].
12	Zinc Calcium Phosphate (ZCP)	Biocompatibility, Osteogenic properties [49, 50].
13	Zinc - Hyaluronate (ZnHA)	Biocompatibility, Promotes wound healing [51].
14	Zn-doped hydroxyapatite (Zn-HAp)	Biocompatibility, Enhanced bone regeneration [52, 53].
15	Mg-Zn-Y-Nd	Biocompatibility, Mechanical strength, and Resistance to corrosion [54].
16	Zn – Al	Biocompatibility, Corrosion resistance [55].
17	Zn – Cu – Fe	Biocompatibility, Antibacterial properties [62].
18	Mg - Nd - Zn - Zr	Biocompatibility, Corrosion resistance, and Mechanical strength [70, 72].
19	Ta-W	Mechanical Strength [84].
20	Ta-Ni-Nb	Super Alloy, Advanced Mechanical Strength, Increased Temperature Resistance [86, 87].
21	Ta-Nb	Weight Reduction, Cost Reduction, Corrosion Resistance [88].
22	Tantalum Pentoxide	Dielectric Properties, Chemical Stability, High Reliability, High X-ray attenuation, Strong Contrast Enhancement, and High Cellular Uptake [89, 90].
23	Tantalum Nitride	Low Contact Resistance, Coverage [92].
24	Ti-Ta-Nb Medium Entropy Alloy (MEA)	Higher Wear Resistance, Greater Biocompatibility [93, 94].
25	Ti-10Ta-6Nb MEA	Higher Hardness, Superior Bio- Corrosion Resistance [95, 96].
26	TaON	Hydrophobicity, Antimicrobial properties [99, 100].
27	PEEK/CS/PTa	Interbody Fusion Efficacy, Biocompatibility, and Bony Fusion Performance [101].
28	TaOx Nanoparticles	Cell Viability, Cell Migration, Cell Attachment, Odontoid/Osteogenic Differentiation, Radiosensitizer, Decreased Cardiotoxicity and Hepatotoxicity [102, 103].
29	Tantalum Composite with Calcium Phosphate Ceramics	Bioactivity, Biodegradability [105].

30	Tantalum Sulphide	Excellent Photothermal Conversion Efficiency, CT Imaging Contrast Agent [108, 109].
31	Tantalum Carbide	Electrochemical Activity, Sensitivity, Selectivity, Stability [111 - 114].
32	Ta/W/Re Matrix with TaC Reinforcement	High Strength, Resistance to Corrosion, Excellent Biocompatibility, Durability [115, 116].
33	Tantalum Oxide + Phosphonic Acid-Carbon Nanotubes	Surface Hardness, Wear Resistance, Corrosion Resistance, Longevity [117].
34	Silver-tantalum-oxide	High Hardness, Wear Resistance, Longevity, Durability, Antibacterial Properties, Biocompatibility, Cell Adhesion [119 - 122].
35	Hydroxyapatite/Tantalum composite	Osseointegration, Long-term Stability [124, 125].
36	Tantalum - PHA composite	Antimicrobial properties, Cell adhesion, Proliferation, Biodegradability [127].
37	Ti35Zr15Nb25Ta25 MEA	BCC structure, Tensile ductility, Yield strength, and reduced weight [129 - 132].
38	Ti-Ta	Compressive strength, Biocompatibility, Open-pore design, Osteogenic effects [135].

3. ZINC AND ITS ALLOYS

3.1 Orthopaedic Application of Zinc and its Alloys

The study focuses on the use of magnesium-zinc (Mg-Zn) alloys in rabbits for various applications, including bone implant stability and reducing complications. The addition of yttrium and manganese to these alloys significantly reduced their degradation rate and improved their mechanical properties. The addition of calcium to the zinc-based biomaterial also improved its mechanical properties while maintaining its biocompatibility and biodegradability [9 - 12].

The importance of hydroxyapatite (HA) as a bone implant material and the advantages of incorporating zinc into it were investigated. The addition of zinc to HA improved its mechanical properties and cytocompatibility, and the alloy had a relatively slow degradation rate in the physiological environment [13 - 15].

The study also investigated the use of zinc oxide nanoparticles as a coating material for implants, which could enhance osseointegration and reduce the risk of bacterial infection. Zinc is crucial in bone growth and regeneration, and its incorporation into bioactive glass materials has potential applications in orthopedics and dentistry [16 - 19].

The addition of silver and zinc doping to the bioceramic layer significantly improved its physical and chemical properties, including hardness, adhesion, and bioactivity. The development and implementation of biodegradable metallic wires, such as magnesium, iron, and zinc, require improved control over degradation rates and biocompatibility [5, 20].

A composite coating consisting of polypyrrole (PPy) and zinc oxide (ZnO) was used to enhance the corrosion resistance, biocompatibility, and antibacterial properties of magnesium alloys. The biocorrosion behavior of zinc alloys is a critical factor in determining their long-term performance in the body, and proper design and testing of these materials are essential for their safety and efficiency [21, 22].

As shown in figure 4, the biodegradable composite material combining zinc matrix and beta-tricalcium phosphate (β-TCP) reinforcement for orthopedic implant applications improved mechanical properties, exhibited good biocompatibility, and was used as antibacterial coatings for titanium surfaces. Zn-Mg-Mn composites with PLA/HA/TiO2 coatings showed good mechanical properties and bioactivity [23 - 25].

Figure-4. Orthopaedic application of Zinc [24].

The study examines the problem of bone infections caused by methicillin-resistant Staphylococcus aureus (MRSA) and the need for effective treatments. Biodegradable zinc alloys were used as implant materials due to their biocompatibility and in vivo degradation. The developed implants have good mechanical properties, antibacterial activity against MRSA, and promote osteogenic differentiation of bone cells. The addition of zirconium and hot extrusion significantly improved the mechanical properties of MgZn1.2 alloys, making them suitable for orthopedic applications. The limitations of existing bone graft materials were identified, leading to the development of composite materials made from HA and Zn-functionalized starch. The Mg-Zn-GO nanocomposites were also identified as promising materials due to their biocompatibility, biodegradability, and osteogenesis promotion. The importance of scaffold design in tissue engineering is highlighted, with Zn-1Mg alloys showing promising results in their biodegradable scaffolds [26 - 30].

3.2 Dental application of Zinc and its Alloys

Voltammetry, an electrochemical technique, was used to detect mercury levels in dental amalgam samples. Zinc oxide-eugenol (ZOE) is a temporary restorative material used for temporary restorations, but its impact on permanent restoration bonding strength is not well understood. The shear bond strength test was used to measure bond strength, but the presence of ZOE significantly reduced the bonding system's strength due to the eugenol in ZOE, which inhibits polymerization [31, 32]. Pulp inflammation is a common issue in dental patients, and CuZnSOD, an antioxidant enzyme, has anti-inflammatory properties. It significantly reduces pulp inflammation, reducing oxidative stress and inflammation in pulp tissue. The selection of appropriate cement or adhesive is crucial for orthodontic treatment, as it provides strong, durable bonding, is biocompatible, and is easy to use. There are various types of cement and adhesives available, including glass ionomer cement, resin-modified glass ionomer cement, composite resins, and self-etching primers. Age-hardening is an important mechanism for improving dental alloy mechanical properties. The microstructural properties of Au-Cu-Zn alloys for dental applications were studied using high-resolution transmission electron microscopy (HRTEM), which revealed tiny, finely distributed particles with a face- centered cubic (FCC) crystal structure [33 - 36].

The figure 5 shows the dental application of a zinc alloyed prosthetic tool. The galvanic currents between gold and amalgam discs were measured using a specially designed galvanic cell. Zinc concentration, surface treatments, and exposure periods all had an impact on how well gold interacted with amalgam. Galvanic currents were affected by surface treatments and increased with zinc concentration. An amalgam devoid of zinc could lessen the contact. In vitro testing was done to determine the possible cytotoxicity of latex and non-latex orthodontic elastics on neuronal cells. Although latex elastics had more noticeable effects, both elastics were significantly cytotoxic. The optimal powder/liquid ratio for zinc oxide-eugenol-based root canal sealers was determined using a standardized method. The powder/liquid ratio increased setting time and compressive strength, while solubility and dimensional stability decreased [37 - 39].

Figure-5. Dental application of Zinc [37].

The study investigates the impact of zinc oxide-eugenol (ZOE) temporary cement on bond strength in an all-in-one adhesive system for bovine dentin. The presence of ZOE temporary cement significantly reduced bond strength, with a 30% decrease in the ZOE group compared to the control group. A new dental alloy with $Au_{61.5}Ag_{16.5}Cu_{12.5}Zn_{6.5}Sn_{2.5}$ was synthesized, exhibiting high mechanical properties and biocompatibility. Zinc polycarboxylate dental cement effectively controlled BAC release, exhibiting potent antimicrobial activity against both bacteria strains. A resin adhesive containing zinc methacrylate showed potent antibacterial activity against Streptococcus mutans, reducing bacterial growth and exhibiting favorable mechanical properties [40 - 43]. The study evaluates the physio-chemical and mechanical properties of cement orthophosphate zinc, a dental biomaterial, and its impact on orthodontic wires. The study reveals that cement orthophosphate zinc has favorable properties for dental applications, with a short setting time, neutral pH, high compressive strength, and low solubility. Additionally, the study examines the effect of zinc oxide nanoparticles (ZnO NPs) on orthodontic wire friction reduction, revealing a uniform and continuous ZnO NPs layer on the wire surface. The study also investigates the effect of zinc-modified titanium surfaces on the osteoblastic differentiation of dental pulp stem cells (DPSCs) in vitro, revealing higher ALP activity and calcium deposition [44, 45, 46].

A zinc-containing desensitizer was synthesized to inhibit bacterial biofilm formation and root dentin demineralization. It significantly reduced demineralization of root dentin by acid-producing bacteria. A zinc-based particle with ionic liquid was used as a hybrid filler for dental adhesive resin, improving mechanical properties and reducing modulus of elasticity. Zinc-silver-based alloys offer promising mechanical properties, biocompatibility, and degradation behavior, making them a promising alternative to traditional metallic biomaterials [47, 48, 49].

3.3 Drug Delivery Application of ZINC and its Alloys

Wilson's disease, a rare autosomal recessive disorder affecting copper metabolism, was first treated with penicillamine, trientine, and zinc. However, penicillamine had significant side effects and was not effective in all patients. Zinc sulfate, a less toxic alternative, showed promising results in preliminary studies. After six to five years, 27 patients with Wilson's disease were treated with zinc sulfate, which improved liver function tests and reduced serum copper levels. Zinc sulfate was well-tolerated by all patients, with only a few experiencing minor gastrointestinal side effects. Zinc sulfate is a safe and effective alternative to penicillamine in treating Wilson's disease, especially in mild to moderate cases [50].

The study investigated the effectiveness of liposome formulations in delivering zinc (II)-phthalocyanine (ZnPC) to serum proteins in vitro and in vivo. The importance of targeted delivery of photosensitizers in photodynamic therapy (PDT) for cancer treatment is crucial, as their nonspecific distribution can damage healthy tissue. The liposome formulations developed in this study have the potential to be used in targeted photodynamic therapy for cancer treatment [51].

As shown in figure 6, the study also explored the potential of starch-graft-poly (acrylic acid) copolymers and starch/poly (acrylic acid) mixtures for peptide drug delivery. The St-g-PAA copolymers and St/PAA mixtures inhibited trypsin activity, suggesting their potential for protecting peptide drugs from proteolytic degradation. They also bind calcium and zinc ions, potentially enhancing the absorption of peptide drugs in the gastrointestinal tract. The study also examined the effect of ethanol on liquid-liquid extraction (LLE) in monosegmented flow analysis (MSFA) for determining zinc in drugs. The addition of ethanol to the organic phase improved the extraction efficiency of zinc, likely due to increased solubility in the ethanol-containing organic phase. The method was found to be accurate and precise, and the MSFA-LLE method was faster and required fewer samples and reagents compared to conventional LLE methods [52, 53].

Figure-6. Drug delivery application of zinc [52].

The study investigates the magnetic properties of Ni-Zn spinel ferrite nanoparticles for potential use in biomedical applications, such as magnetic resonance imaging, magnetic hyperthermia therapy, and targeted drug delivery. The synthesized nanoparticles exhibit superparamagnetic behavior with high magnetization value and low coercivity, making them attractive for these applications. They also have potential applications in nano-bio fusion, as contrast agents for magnetic resonance imaging, magnetic sensors for biological applications, and magnetic carriers for targeted drug delivery [54, 55].

A study developed a magnetic nanoemulsion loaded with zinc phthalocyanine (ZnPC) for use in photodynamic therapy (PDT) of skin cancer. In vitro experiments demonstrated high retention in skin layers and phototoxicity towards melanoma cells, suggesting potential for PDT of skin cancer. Two well-characterized particles, alpha-quartz, and nano zinc oxide, were used as benchmarks for toxicity screening of inhaled nanoparticles for drug delivery. These particles have been extensively studied for their toxicological effects and can provide a standardized reference for comparison of new particles [56, 57].

Zinc oxide nanoparticles have great promise for the targeted killing of tumour cells and medication delivery. They can cause apoptosis, damage cell membranes, and produce reactive oxygen species. They also have physical characteristics including size, shape, and surface charge. For the administration of medications and the imaging of living cells, fluorescent porous zinc sulphide (ZnS) nanospheres have been created. Utilised for intestinal insulin administration, alginate-coated zinc calcium phosphate (ZCP) nanoparticles have the potential to preserve insulin against deterioration and enhance oral bioavailability. Utilising X-ray diffraction, scanning electron microscopy, and transmission electron microscopy, ZnO nanoparticles of various sizes have been studied. Levodopa, a medication frequently used to treat Parkinson's disease, has been delivered using layered double hydroxides (LDHs) nanoparticles. Nanosized cross-linked sodium hyaluronate (NaHA), linear NaHA, and zinc- hyaluronate (ZnHA) have been investigated as mucoadhesive drug delivery systems for ocular drug delivery. The release of a model drug, dexamethasone, from the nanoparticles can be controlled by varying the degree of cross-linking and the presence of zinc ions [58 - 63].

New drug delivery systems are needed to improve the efficacy of anticancer drugs. Surface-functionalized cobalt and zinc ferrite nanohybrids have shown potential in delivering curcumin to MCF-7 breast cancer cells, improving drug-loading capacity and release profiles. ZnO-based nanocarriers have been developed for passive and smart strategies, with passive drug delivery strategies such as physical adsorption, electrostatic interaction, and encapsulation. Zn-doped hydroxyapatite (Zn-HAp) nanoparticles loaded with doxorubicin (DOX) have shown higher anti-cancer activity and sustained drug release profiles. Self-propelled microrockets made from poly (aspartic acid)/iron-zinc have also shown potential for targeted drug delivery in the stomach [64 - 67].

Zinc-doped magnesium ferrite nanoparticles have been synthesized using various methods, including co-precipitation, SEM, TEM, and XRD. These nanoparticles exhibit anticancer activity and potential drug delivery applications. Zinc oxide nanoparticles have anticancer properties and are used in targeted drug delivery, sustained release, and imaging. Zinc-faujasite zeolites have potential as a drug delivery system for 6-mercaptopurine, a drug used in leukemia and inflammatory bowel disease. Zinc-silver nanocages also act as wound-healing agents, promoting cell proliferation, migration, and collagen deposition [68 - 71].

3.4 Stents Application of Zinc and its Alloys

Zinc plays a crucial role in cellular proliferation, differentiation, and extracellular matrix production and its potential therapeutic effects in vascular injury are being studied. Zinc may inhibit smooth muscle cell proliferation and migration by regulating cell cycle proteins, cytokines, and growth factors. The coating procedure and nickel release of nickel-tungsten amorphous nanocomposites coated with PUMC zinc/calcium phosphate significantly reduce nickel release in human cell cultures, improving corrosion resistance and reducing cytotoxicity. Low- Low-temperature hydrothermal growth of zinc oxide (ZnO) nanorods on stents has been studied for cell adhesion and viability, resulting in improved adhesion and viability of smooth muscle cells. These nanorods have no cytotoxic effects and may reduce the risk of restenosis and thrombosis [72 - 74].

As shown in Figure-7, the study of microstructure and corrosion properties of a sub-rapid solidification Mg-Zn-Y-Nd alloy shows significant improvements in the alloy's microstructure, resulting in a fine and homogeneous distribution of elements. The alloy has good corrosion resistance in dynamic simulated body fluid and a low corrosion rate, making it potential for use as a biodegradable vascular stent material. In vitro and in vivo degradation behavior and biological response of new biodegradable Mg-Y-Zn alloys show slower degradation rates and more stable corrosion behavior. The addition of neodymium (Nd) to extruded Mg-2Zn-0.46Y-xNd alloys improves the microstructure and mechanical properties, increasing yield strength, ultimate tensile strength, and corrosion resistance [75 - 77].

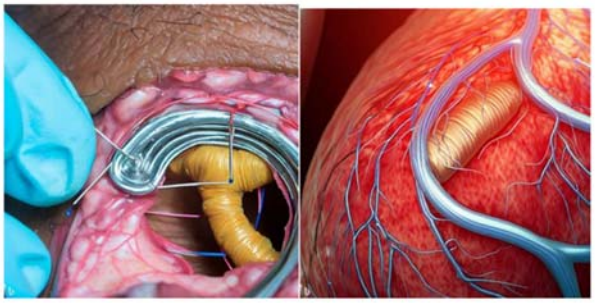

Figure-7. Stents application of Zinc [75].

Cyclic extrusion compression (CEC) treatment improves the microstructure and properties of Mg-Zn-Y-Nd alloy, reducing grain size and precipitates. It also increases yield strength, ultimate tensile strength, and elongation. CEC treatment does not significantly affect corrosion resistance. Zinc is ideal for bioabsorbable stent applications, with a slower corrosion rate than magnesium and iron. CEC processing results in high strength, ductility, and low corrosion rate in simulated body fluid. A new magnesium alloy (Mg-Nd-Zn-Zr) with MgF2 coating significantly enhances bioactivity, hemocompatibility, and corrosion resistance, reducing magnesium ions release and preventing cell viability issues [78 - 81].

Both in vitro and in vivo studies have looked at zinc as a potential component for bioabsorbable stents. In comparison to other metals like iron and magnesium, the study discovered zinc to have minimal cytotoxicity, and zinc stents that had been inserted were completely absorbed after six months with no negative effects on the tissue around them. New zinc-based alloys that demonstrate superior mechanical qualities and corrosion resistance in physiological settings were created. These alloys also have better mechanical and degradation properties. Different Zn-Cu alloy samples with varying Cu levels exhibited strong mechanical characteristics and corrosion resistance, with an increase in Cu content leading to a decrease in corrosion rate. The study also examined how pure zinc stents in rabbits degraded, finding that the rate of deterioration was initially high but steadily decreased over time, with the stents remaining intact after a year [82 - 85].

The study aimed to design and fabricate Zn-Al alloys with varying Al contents, evaluate their strength, ductility, and corrosion resistance, and assess their biocompatibility in vivo. The study also explored magnesium and zinc-based alloys as biodegradable materials for vascular stent applications. The Zn-Cu-Fe alloys showed good cytocompatibility, hemocompatibility, and antibacterial properties, indicating potential use for preventing stent-associated infections. Both Zn-Mg and Zn-Cu alloys have similar mechanical properties to existing biodegradable metallic materials, and their in-vitro degradation behavior showed gradual degradation over time [86 - 89].

4. TANTALUM AND ITS ALLOYS

Tantalum, first used in dental implants in the 1950s, has become increasingly popular in medical devices like hip and knee replacements, heart pacemakers, and blood vessel tubes. Its biocompatibility makes it suitable for use in the body due to its strength and stiffness, making it ideal for supporting weight in hip and knee implants. Scientists are working to improve tantalum's surface and fit in with the body's tissues by using methods like rough surfaces and special materials to enhance its attachment to bone tissue. This aims to enhance the integration of tantalum implants with bone tissue. The applications covered here are:

1. Medical devices

2. Drug delivery

3. Surgical instruments.

4. Orthopaedic and dental implants.

4.1 Medical Devices

Tantalum was first used in biomedical engineering for medical devices due to its radiopacity and biological inertness properties. It was also used in capacitor leads due to its electrical properties. Studies explore the application of tantalum in medical devices:

Hunter [90] reviewed the use of tantalum in medical devices like orthopaedic implants and cardiac pacemaker leads. Tantalum’s biocompatibility, resistance to corrosion, and mechanical properties were reported, for long-term implantation. It was often seen to be combined with titanium or stainless steel to enhance mechanical properties and reduce device weight.

Figure-8. Patient with abdominal wall defect repaired with tantalum mesh [90].

Tantalum is a highly biocompatible, corrosion-resistant, and mechanically strong material used in medical devices like orthopaedic implants and cardiac pacemaker leads. It is often combined with other materials like titanium or stainless steel to improve mechanical properties and reduce device weight. US Patent 5,406,444 describes a method for coating tantalum feedthrough pins to improve performance in all applications. However, tantalum's performance is limited in high-temperature and high-pressure environments, and a refractory metal layer could improve performance. Tantalum is also visible on MRI images, making it suitable for accurate placement and monitoring during MRI procedures. However, some tantalum-containing devices may produce artifacts or distortions, requiring careful consideration of MRI compatibility and visibility before clinical use [3, 90, 91].

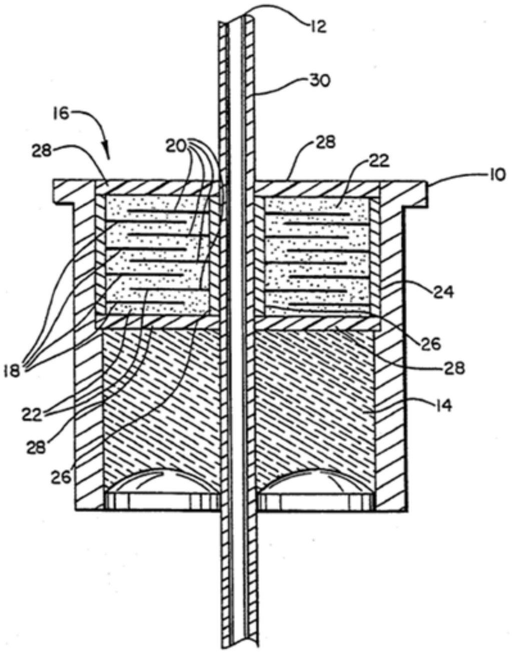

Figure-9. Coated tantalum feed through pin design [3].

US Patent 5,931,818 introduced a method for intraparenchymal positioning of medical devices using electromagnetic fields. Tantalum, a high-atomic number metal, was used as a marker for tracking the device's location, providing real-time feedback. Van Oeveren et al. introduced tantalum as a metal for stent construction, allowing the implantation of tantalum stents and reducing platelet deposition. US Patent 6,283,985 B1 described a method for reforming wet tantalum capacitors in implantable defibrillators, addressing capacitor degradation over time due to "aging." The process can be performed before or after incorporating the capacitors into the device, ensuring long service life and improved reliability. Sarma Mallela et al. highlighted the evolution of pacemaker batteries, shifting from mercury-zinc to lithium-iodine and lithium-silver vanadium oxide batteries, offering longer life and greater reliability. Tantalum is often used for pacemaker components due to its biocompatibility and resistance to corrosion [91 - 95].

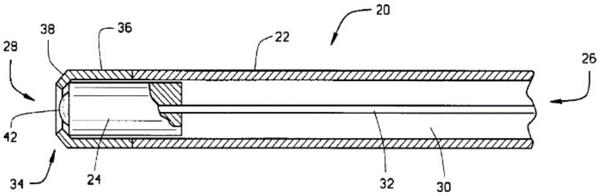

Figure-10. Tantalum marked medical device for intraparenchymal positioning [94]

US Patent US 7,355,242 B2 describes a tantalum anode for high-voltage capacitors in implantable medical devices, addressing high failure rates and corrosion resistance. Kane *et al*. developed the BION implantable neurostimulator, which uses tantalum pentoxide for electrode construction. Tantalum is used as a substrate and coating for the microstimulator's circuitry and electrodes, demonstrating its potential in new implantable medical devices. Freedman and others used Ta2O5 nanoparticles as a contrast agent for X-ray computed tomography (CT) imaging of articular cartilage, demonstrating their ability to overcome limitations and provide high contrast images. Meanwhile, Piestrzynska's group developed a biosensor based on long-period gratings (LPGs) coated with Ta2O5 nanoparticles to make it ultrasensitive. It was for detecting biological targets and achieving successful detection of streptavidin, BSA, and E. coli. Pawelec *et al*. proposed using tantalum oxide nanoparticles as radiological markers for implantable device tracking and performance using X-ray imaging [6, 96, 97].

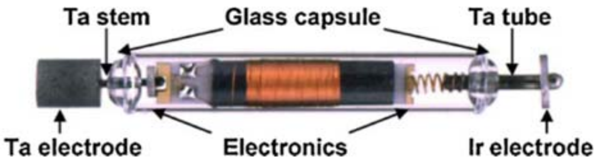

Figure-11. BION microstimulator [6].

4.2 Drug Delivery/ Pharmaceutical

Tantalum is seen to be widely used in biomedicine for drug delivery systems and pharmacology. This is because it can work in combination with other elements. Studies have shown that tantalum in combination with hyaluronans is a potential drug delivery system. Cox et al. found that local delivery of heparin and methotrexate with tantalum-based drug delivery systems can reduce neointimal proliferation in stented arteries. US patent 5383928 describes a stent sheath for delivering drugs to blood vessels, focusing on the design, reservoir, and mechanism for drug release.

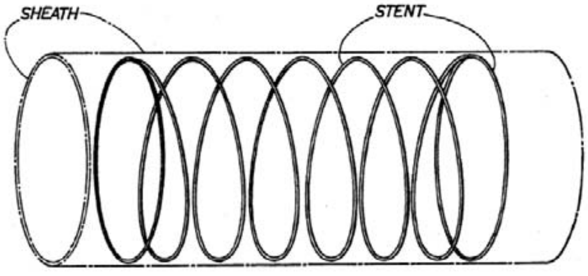

Figure-12. Tantalum Stent sheath for drug delivery [98].

Lincoff *et al*. developed a stent system using tantalum to release dexamethasone, an anti-inflammatory steroid, into the surrounding tissue. The system effectively reduced neointimal hyperplasia and was well-tolerated by porcine subjects. Arrudo et al. highlighted the potential of drug delivery systems of tantalum bases in orthopaedic implants and nanoparticles for targeted drug delivery. Guo's group developed a novel approach to use porous tantalum implants for sustained drug delivery by electrostatically assembling multilayer copolymeric membranes and loading them with chemotherapy drug doxorubicin. The membranes effectively controlled the release of doxorubicin over several weeks, demonstrating significant anticancer activity against cancer cells and inhibiting tumor growth in a mouse model. Bose and Tarafder discussed the use of calcium phosphate ceramics as carriers for growth factors and drugs, enhancing their bioactivity and biodegradability [98 - 101].

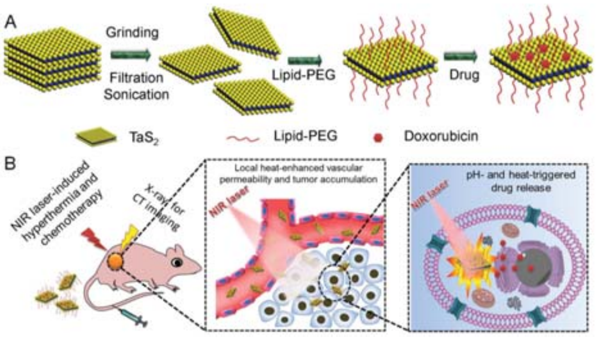

Figure 13. Effective and safe cancer therapy using PEG- TaS2 NS platform [104]

Tantalum-based catalysts have shown promise in polymerizing lactides and ε-caprolactone. This gives high molecular weight polymers of narrow distributions. These catalysts can aid the synthesis of biodegradable polymers by providing precise control towards ring-opening solvent-free polymerization. Mesoporous tantalum oxide nanoparticles can effectively load chemotherapy drugs doxorubicin and iodinated oil, enhancing their anticancer effects in the lab as well as patient trials. Liu and others reported that tantalum sulphide nanosheets can load and release antibiotics, demonstrating their potential as a drug delivery agent [102 - 105]. Tantalum can also be used in computed tomography as a contrasting agent that inhibits tumor growth and improves survival rates. 3D-printed porous tantalum scaffolds have excellent biocompatibility, mechanical strength, and porous structure, ideal for bone tissue engineering and drug delivery systems. Ta2O5 nanoparticles have high X-ray attenuation properties, making them highly effective as CT contrast agents. The synthesized oval-shaped Ta-C/f-MWCNT composite exhibited excellent electrochemical activity and good sensitivity for detecting nitrofurantoin, with good selectivity and stability [106, 107].

4.3 Surgical Instruments

Tantalum is increasingly used in biomedical engineering for surgical instruments, sutures, and clips. Studies show that tantalum and titanium can reduce surgical time, increase precision, and improve cosmetic outcomes. Metal clips are faster and compatible with MRIs, while tantalum is safe for use during MRIs due to its non-magnetic nature. US patent 5030218 describes an electrosurgical instrument with a composite blade made of tantalum, rhenium, and titanium, with high melting point, strength, and corrosion resistance [108 - 110].

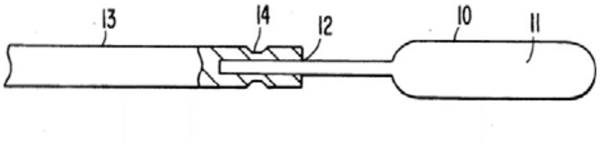

Figure-14. Electrosurgical instrument with tantalum composite blade [110].

Cardonne *et al.* discuss the use of tantalum in various fields because of its various relevant properties, including compatibility in biological applications, resistance to corrosion, and high purity. They describe a surgical stapling device with a composite material cartridge, featuring a matrix material made of titanium, zirconium, hafnium, niobium, tantalum, and alloys, and a reinforcement material made of carbides of W, Ti, Ta, and Mo. The device attaches one layer of material to another during surgical procedures, using a wire guide and suture wire [111 - 113].

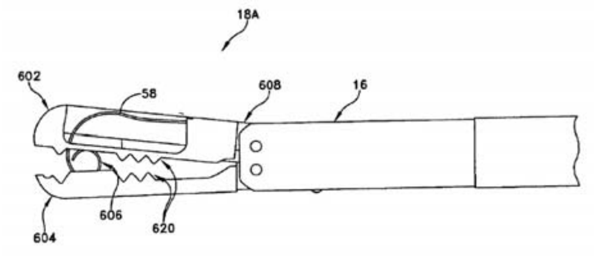

Figure-15. Surgical suturing device [113].

Maccauro *et al*. explored utilization of tantalum, particularly in surgical equipment. Tantalum has excellent biocompatibility, high corrosion resistance, and strength, and thereby, is a promising material for bone and teeth implants, drug delivery systems, and further research. Maho et al. synthesized coatings using carbon nanotubes modified by tantalum oxide and phosphonic acid. This improved titanium surfaces' hardness, and resistance to wear and corrosion. Alias et al. explored the use of nanostructured thin films based on silver-tantalum-oxide on stainless steel 316L for tools of surgery, demonstrating high hardness, wear resistance, antibacterial properties, and biocompatibility [114 - 116].

4.4 Implants

Tantalum has been extensively researched and developed for various applications in biomechanics and medicine practices, including but not restricted to bone, tissue, and dental implants. Its porosity, biocompatibility, osseointegration, and biomechanical properties make it a promising material for implants. Studies have shown that porous tantalum has high bone ingrowth, excellent biomechanical properties, and optimal bone-implant fixation. Björk's method is preferred for the superimposition of serial-cephalometric radiographs, while Ricketts' method is more accurate for growing subjects. Tantalum has also been used in hernia surgery, with its durability and inert nature making it ideal for hernia repair prosthetics until plastic gauzes became popular. Porous tantalum implants have shown improved patellar tracking, increased range of motion, and decreased pain in most patients, making it a promising option for revision and salvage patellar arthroplasty [117 - 120].

Fathi and Azam studied a novel coating on metallic dental implant surfaces. It combined hydroxyapatite with tantalum. The coating improved implant osseointegration and success rates compared to uncoated implants. Tantalum is a low modulus metal with a cancellous bone appearance. Hence, it is used in orthopaedic surgery for arthroplasty, and spinal surgery, and substitutes for the bone graft. Its biocompatibility, high corrosion resistance, and strength have made it a promising material for orthopaedic and dental implants, drug delivery systems, and surgical equipment research [121 - 123].

Figure-16. Different possible implants using tantalum [123]

Liu *et al*. studied the effectiveness of using a porous tantalum rod for treating femoral head necrosis, finding better outcomes in pain relief, hip function, and radiographic assessment compared to traditional treatment. Their study stated that a porous rod of tantalum is a safe and effective treatment option for early and intermediate-stage ONFH. Bencharit and others noted the use of tantalum to improve as well as facilitate osseointegration of dental implants, highlighting its success in orthopaedics. Liu’s group compiled the physical, chemical, mechanical, and biological properties of tantalum and suggested surface modifications for improvement. However, further evidence and deeper study need to focus on the effects of porous tantalum’s properties on human safety [124 - 126].

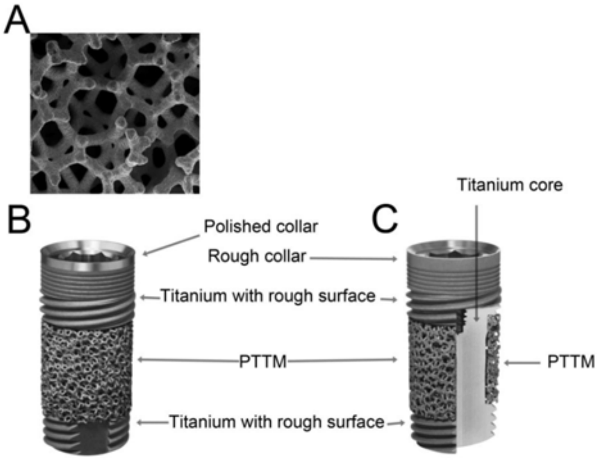

Figure-17. Porous tantalum trabecular metal on titanium core [125].

Tantalum is used in orthopaedic surgery, and George and Nair evaluated its synthesis, structure, and mechanical characteristics. They mentioned several clinical procedures, such as tumour reconstructive surgery, osteonecrosis, cranioplasty, foot and ankle surgery, hip and knee replacement, and spine fusion. The authors urged more research and covered risk concerns related to tantalum use in orthopaedics. To prevent biomaterial-associated infections, Rodriguez-Contreras and others devised antimicrobial coatings for implants of tantalum [127–130]. Liu's research group investigated porous tantalum for osteonecrosis in the repair of articular cartilage and subchondral bone. Beline *et al*. studied magnetron sputtering parameters in tantalum oxide films, finding high optical homogeneity, roughness, and surface energy values. Patel et al. found tantalum to show promising results in spinal surgery, cervical surgery, and lumbar surgery. Chen *et al*. compared the biological corrosion and biocompatibility of TiTaNb and Ti-10Ta-6Nb films, finding superior bio-corrosion resistance. Li's group summarized the progress in the physical, chemical, and biocompatible properties of tantalum, proving its excellent corrosion resistance [131 - 133].

Yakovin and others investigated the antimicrobial effect and resistance to thrombosis of tantalum oxynitrides, while Mustafi et al. reported a new biocompatible Medium Entropy Alloy (MEA) called Ti35Zr15Nb25Ta25. The MEA was lighter and stronger than pure Tantalum, making it the most biocompatible metal. NeoMTA 2, a novel material created for vital pulp treatment or perforation repair, was examined by Rodriguez-Lozano et al. for its biological effects and biomineralization potential [134-138]. Tantalum has been developed for bone implants because of its superior corrosion resistance and osteo-regenerative qualities, according to Putrantyo et al. The development of porous tantalum in bone-tissue implants and the clinical use of tantalum-based implants for patients needing particular prosthesis and implants were both covered by Huang et al. Tantalum and its alloys' biological and material qualities were evaluated by Mani *et al*., who provided evidence for its safe usage in implants and medical equipment. Ti-Ta bone scaffolds were successfully produced via additive manufacturing, according to Soro *et al*. [139, 140].

Lei *et al*. improved Ti6Al4V-Ta alloy scaffolds by directly additive manufacturing porous tantalum using Laser Powder Bed Fusion. They tested biocompatibility and mechanical properties using rat bone marrow cells and rabbit femur, revealing good mechanical and biocompatibility. Chen et al. studied tantalum's anti-infective and antibacterial properties, finding a mechanism for its antibacterial effects. Yuan et al. quantified important fundamental biocharacteristics of a PEEK/CS/pTa cage in a goat model, finding it similar in bony fusion performance and biologically safe. Huang et al. explored the impact of inherent material structure and characteristics on scaffolds of tantalum-titanium alloy. They found diamond structure scaffolds had moderate mechanical strength and excellent osteogenesis, while rhombic dodecahedron scaffolds displayed superior mechanical properties and moderate osteogenic effects [141 - 144].

5. MAGNESIUM AND ITS ALLOYS

5.1 Osteosynthesis Application

The ability of magnesium or its alloys to function as orthopedic implants. Due to its favorable mechanical characteristics, such as density, Young's modulus, and compressive strength, which are all equivalent to those of real bone, magnesium (Mg) is now used in biodegradable osteosynthesis materials for bone repair [147]. Mg is a particularly good option for the creation of various medical devices, such as bone substitutes, temporary pro-regenerative scaffolds for bone, and osteosynthetic plates and screws because it possesses mechanical strength that is comparable to that of human cortical bone [148]. To create excellent alloys with great room-temperature stability, the mechanical characteristics of magnesium can be combined with those of other metals [145].

As prospective Mg implants for musculoskeletal applications in 1900, Payr proposed nails, fixator pins, cables, pegs, tremors, Magnesium sheets, and plates [146, 147, 148]. Payr also mentioned the use of an Mg peg as an intramedullary stabiliser in the treatment of pseudoarthrosis and incurable broken bones [149]. A 17-year-old boy with a complex pseudoarthrosis and significant malalignment of the distal third of the lower leg as a result of a lower leg fracture that had occurred two months earlier was the subject of Lambotte's initial study with magnesium implants in 1906 [150]. The initial use of an iron sheet with an iron bolt fastening by Lambotte led to clinical failure [151].

After months, Lambotte had a second excision of the injury tips while stabilising the fracture using an exterior repair approach. Lambotte opted to use an iron cable cerclage for the fibula and a Magnesium sheet with six metal bolts at the tibia to repair the fracture. The day after the last treatment, the child had multiple subcutaneous gas cavities, localised edoema, and pain. Later, Lambotte withdrew the magnesium sheet in tiny pieces because of the excruciating pain. Lambotte employed a bone graft from the top of the asymmetrical tibia to treat the injury [151].

Lambotte was startled by this clinical incident and later discovered that the magnesium dissipated as a result of an electrochemical reaction between the magnesium sheet and the steel bolts. He decided to use animal research to investigate this phenomenon along with his assistant Verbrugge. Between 7 and 10 months, they discovered complete magnesium resorption in rabbits and dogs [151]. Lambotte was inspired to carry out more clinical research because of complete Mg absorption and the absence of postoperative discomfort. Because pediatric supracondylar fractures heal fast, he chose to treat them. Additionally, with remarkable accuracy, he was able to implant a Magnesium spike with a smaller implant size. Four kids (7-10 yrs old) with supracondylar humerus injuries had been operated on by Lambotte and Verbrugge; all of them made a full recovery (with the exception of an air leak).

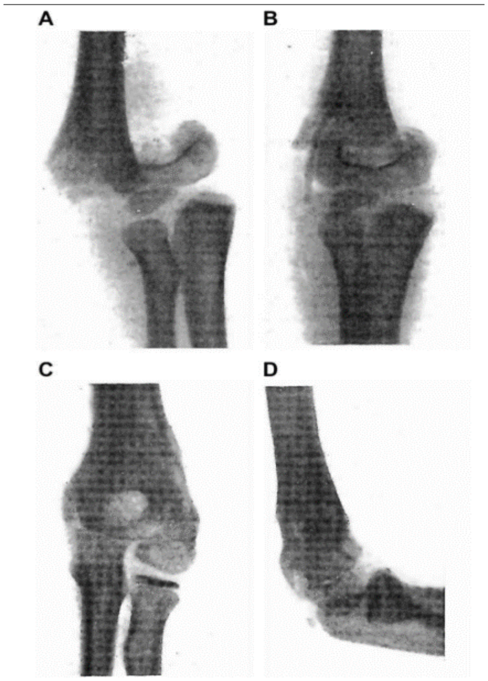

Figure-18. By Lambotte depicts a child's fractured supracondylar humerus (A) after it had been fixed with a magnesium nail (B). After the metal spike had totally rusted for many months, the crack was steady as shown in the two surface X-rays (C and D). There was no discomfort or infection. The child's elbow performed well clinically [151].

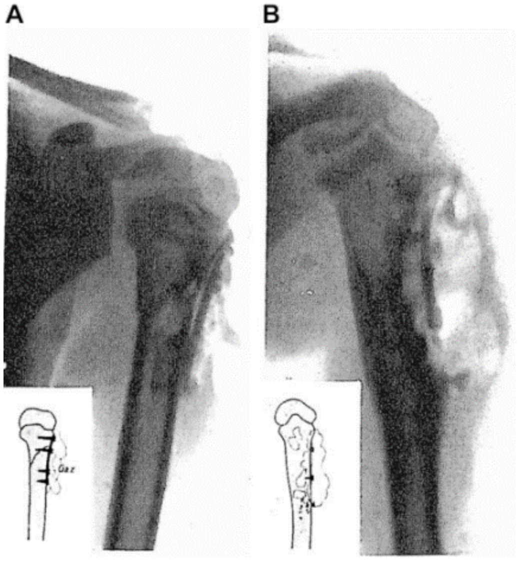

Figure-19. Shows how Verbrugge used a magnesium plate and screws to stabilise a diaphyseal humerus injury in a child who was eight years old. The metal plate had mostly corroded after three weeks, according to postoperative X-rays in (A) that reveal previously generated gas cavities and (B) [151].

He waited over a year after treating the first 7- 7-year-old kid to evaluate the clinical outcomes before treating the next batch of kids. In these cases, Lambotte observed total Magnesium resorption a year following operation and physiological (according to X-rays) bone healing without any hypertrophy bones. To pursue his clinical investigation, Lambotte operated on an 8-year-old boy who had a trans diaphyseal humerus fracture [152]. Later, Verbrugge noted that this young patient had received Mg plate and screw fixation (Figure-4A) treatment. The metal plate nearly totally disintegrated three weeks after the surgery, and the bone fracture line was no longer visible.

Resorbable Mg plates and screws appeared to be the optimal osteosynthesis material, according to Henschen and Gerlach's assessment from 1934 [153]. However, there were additional conclusions that largely relied on animal testing and were unfavorable of the use of mg in bone uses. In his 1913 report of his studies on rabbits, Burrows disapproved of the use of mg since it appeared to produce abscess cavities and dissolved too quickly to be beneficial for stabilising the shattered fragments [154]. He investigated magnesium metal as an intramedullary pin [155]. Magnesium operates largely as a connective tissue stimulant, according to Zierold's analysis of the effects of numerous metals on tissue in bones in 1924. Zierold also hypothesised that mg may have other effects.

Verbrugge was aware of Zierold and Groves' critical claims and findings regarding the use of magnesium in bones. However, while serving as Lambotte's assistant, Verbrugge investigated a 2.5 mm solid pure Mg tube in the femura of bunnies and dogs [157]. Under a modest gas evolution, the Mg cylinders corroded gradually over 4 months. After 4 months, the Mg cylinders continued to withstand finger pressure, according to Verbrugge [157]. He saw that the magnesium cylinders became hollow and brittle after six months. There were no indications of tissue irritation or inflammation in the surrounding tissue [157]. After three weeks, there was no response; however, after seven weeks, there was a bigger reaction, which eventually went away after a few months. Verbrugge said that the concomitant gas production had not caused any tissue injury.

Verbrugge conducted his clinical investigation on 21 clinical cases using the Dow alloy Mg 8 weight percent Aluminium and an Elektron alloy (Mg alloy). During the eighth postoperative phase, Verbrugge saw hydrogen cavity creation without any negative clinical effects [158]. Every patient had normal body temperatures and showed no additional symptoms of illness. No harm was done to the body, ligaments, bones, or joints by the corroding magnesium. The periosteal reaction was as important as with traditional non absorbable prostheses or conventional therapy. According to Verbrugge, the implanted magnesium is neither harmful nor irritating.

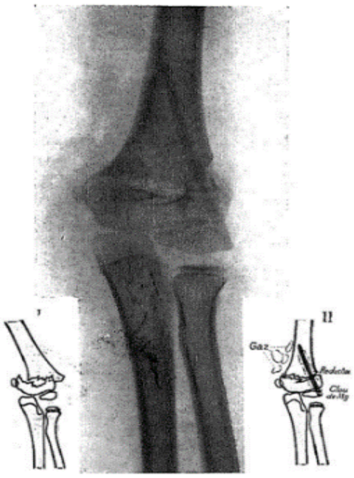

Figure-20. Verbrugge displayed a supracondylar postoperative X-ray. A Dow magnesium nail was used to cure a child's fracture who was 7 years old [152]. It is possible to witness the early stages of subcutaneous gas production [158].

After speaking with Jean Verbrugge personally, McBride became interested in his work in Antwerp in 1938. Verbrugge then gave some basic Mg material to McBride. McBride found that plates made of magnesium metal were unacceptable. Magnesium metal, in his opinion, is not suitable for use as medullar pegs due to its explosive gas-forming action, which demands a break into connective tissue. When placed more snugly into the hard cortical bone, screws are more corrosion-resistant than plates, according to McBride. The screws should pierce the bone shaft on both sides and contain more magnesium.

McBride used a tap that was the right size for the bolt. He also covered some surgical techniques that were altered to work with Magnesium implants [159]. The Mg bone pegs should have a three-corner design, according to McBridge. He continued by saying that while the Mg alloy is safe, it does produce a localised rupture of the tissue, which limits its usage to circumstances in which absorption is favourable and where the load on the bits will be very little between three and five weeks. McBride agreed with Lambotte and Verbrugge that the possibility of forced electrolytic corrosion made magnesium implants inappropriate for use with other metals. The magnesium alloys used by McBride were stable for three to seven weeks and produced reliable results.

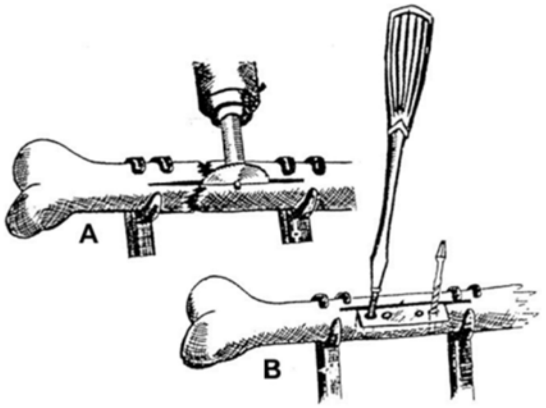

Figure-21. McBride demonstrates a method for creating rotation-resistant osteopathy utilising Mg-Mn as a slender and angled sheets and bolts [159].

Maier evaluated pins made of spindle-shaped Mg sheets in two human humerus injuries in 1940. While the recovery period in one instance went without a hitch, the implant in the other required removal just 12 days after the treatment because gas holes continued to form. After 14 years, Maier saw strong functional results in both cases. It has been said that these spindle-shaped pins are particularly resistant to bending and shear. Maier began doing studies on rabbits in response to his positive clinical outcomes. He placed a strip of magnesium subperiostally into the tibia of a rabbit and watched as the metal corroded, gas chambers formed, and extensive periostal bone formed. He connected these phenomena to the corrosion product's potent irritating impact.

Troitskii and Tsitrin reported on the successful treatment of 34 cases of pseudoarthrosis utilising an implant and bolt combination made of an Mg - Cd alloy in 1948 [161]. The osteosynthesis material was fully absorbed, leaving nothing behind, and this prompted the growth of the callus bone. This bone-stimulating effect was thought to be caused by the MgCO3 generation that was seen in the corrosion layer. Troitskii, Tsitrin, and Verbrugge claim that the implantation of Mg into inflammatory tissue balances the environment's acidity, which afterward encourages the growth of callus bone. To accomplish precise bone repositioning and prompt consolidation of the crack in severe instances, Troitskii and Tsitrin advised utilising an intramedullary rod implant that was particularly designed and constructed of an Mg - Cd alloy.

It's important to note that although Hume-Rothery and Bowell had examined the balance chart of the Mg-Cd system in 1927 [163], Stroganov submitted for a patent in 1969 [160] for alloying Cd to Mg to boost the resistance to corrosion.

Seven individuals with tibial eminence fractures have been observed by us since 2014. Before surgery, patients had a clinical and radiological (MRI, CT scan) assessment. Only 3 patients who initially had a grade III or IV lesions were surgically treated with magnesium resorbable screws for internal fixation. Following surgery, functional recovery was assessed clinically and by X-ray at 1, 2, 4, 6 and 12 months. Scores from the Lysholm and IKDC was provided at 1, 2, 6, and 12 months. At 6 and 12 months, the MRI was repeated [163].

5.2 Features of the Screw

Magnesium screws (MAGNEZIX®, Syntellix AG, Hannover, Germany) are classified as a MgYREZr metallic alloy and have a high resistance to traction, according to DIN EN 1753. The screws' Young's modulus is E = 41-45 GPa and they are countersunk to prevent any prominence on the articular surface. Mechanically, the yield strength, tensile strength, and elongation to failure values of the screws are all greater than 260 MPa, 290 MPa, and 8%, respectively. This implant is eventually vulnerable to corrosion-induced degradation and absorption, unlike polymers, which disintegrate through hydrolysis. The implant is completely and evenly replaced by newly formed bone since it is osteoconductive. Its chemical makeup of magnesium and zinc does not cause stress shielding, and there have been no known dangerous interactions [164].

Figure-22. Pre-operative X-ray assays: case n.1 (A), case n.2 (B) and case n.3 (C).

Figure-23. Post-operative X-ray assessment for cases n.1, n.2, and n.3.

Due to the development of novel implant biomaterials and surgical procedures, bone surgery has advanced recently. The majority of the studies included in this systematic review show that Ti and Mg devices produce functional results that are comparable; however, Mg appears to employ a lower rate of implant removal and problems. The effectiveness and safety of Mg-based al-loy screws appear to be on par with those of conventional osteosynthesis implants, according to the most recent research. It does not appear that a Mg screw is less successful in stabilizing fractures than a Ti screw [165].

The biodegradability of magnesium is a pro for indirect safety since it eliminates the need for further surgery for implant removal. In addition to their biocompatibility, magnesium devices also have osteo-conductivity, which enables complete restoration of the autologous bone after resorption. The putative antibacterial properties of magnesium constitute a last significant benefit. Currently, only tiny implants used to mend bone fragments while avoiding significant mechanical loads may be made with magnesium-based alloys [165].

These fascinating historical facts on the many medical uses of metallic Mg in both humans and animals are described in this study together with the overall findings of the in vivo and in vitro behaviour of Mg-based implants. The results are organised relative to their clinical uses [8]. Magnesium was initially described as an implant material in a clinical paper from 1878 that discussed absorbable ligatures for the closure of bleeding arteries. Several authors from the early 20th century described employing mg and similar alloys as fasteners for shattered bones and materials for quick soluble wound care. Here, magnesium alloys were employed by Payr and Chlumpsky to connect blood vessels and intestines. Payr treated vessel tumors (haemangiomas) with small arrows and magnesium tubes for nerve and vascular sutures. Seelig employed pure magnesium as a general surgical suture material and to ligature blood vessels [166]. While magnesium was being corroded in vivo, he saw significant volumes of subcutaneous hydrogen cavities but no systemic harmful consequences. Clinically, the use of magnesium wires as wound sutures was unsuccessful. A rapid rate of corrosion pushed hydrogen gas through the suture holes, delaying the healing of the wound. When Nicole implanted implants made of only magnesium into soft tissue, she saw significant inflammation around the implants that were corroding terribly. This resulted in an implant that was surrounded by fibrous tissue. Gas cavities were seen infiltrating the surrounding tissue [166].

In the beginning, in 1906, Lambotte employed pure magnesium as fracture fixing plates in musculoskeletal surgery [167]. When he paired a magnesium plate with steel screws, he saw a quick disintegration of the magnesium plate within 8 days. It was the initial demonstration that oxidation contributes to the in-vivo degeneration of mg implants. Hey, Groves tried to mend broken bones using magnesium alloys in 1913 [167]. The magnesium alloys he employed experienced in-vivo corrosion, which resulted in gas holes and an unhealed crack site. However, he did discover that magnesium considerably encouraged the growth of new bone. Verbrugge and McBride, two physicians, repaired human bone injuries effectively using bolts, pins, and slabs made of alloys of magnesium [167]. They also detected gas cavities, but instead of the greater hydrogen gas concentrations predicted by theory, they discovered a gas mixture of 5.6% $CO2$, 6.5% $O2$, 7.3% $H2$, and 80.6% $N2$. For screws and rods, McBride utilized the magnesium alloy $Al4Mn0.3$, and for plates, $MgMn3$. After 120 days, the screws had entirely rusted. There were no systemic harmful effects that he could see. Magnesium rods were employed by Maier, another surgeon, in 1923-1924 to treat upper arm fractures [168]. Although he noted good and rapid fracture healing in every patient, he had to redo certain magnesium rod treatments due to large gas cavities. Based on his medical knowledge, he investigated magnesium plates in bunnies. After 9 days, he saw increased callus mineralization and 18 days after surgery, there was a robust mineralized callus.

Mg as an implant material lost favour once stainless-steel ones were developed at the beginning of the 1940s. Later, just a few studies were released. Early in the 1970s, Stroganov proposed magnesium alloys incorporating cadmium as implants with reduced corrosion rates, particularly for use in bone surgery [169]. Kuwahara proposed using heat treatment to slow down the corrosion of magnesium alloys and pure magnesium. It seems reasonable that how effectively magnesium alloys function in vivo will be influenced by the tried-and-true techniques and therapy options utilised to change their mass and surface properties. Development efforts should concentrate on employing the correct combination of alloying components, manufacturing procedures, and treatment of the surface to produce a magnesium alloy that exhibits slow and typical corrosion in vivo. A new study in the area of biomaterials was prompted by the use of innovative magnesium alloys with rare earth metals as alloying elements. Recent studies on magnesium alloys incorporating rare earth as disposable stent materials for cardiac surgery and as temporary orthopedic implant materials [169] have been conducted.

Initial strong biological compatibility, successful research on animals, and first clinical trials of biodegradable magnesium stent allowed for the development of the first readily available biodegradable magnesium stent. For the utilisation of alloys of magnesium in hard cells, further fundamental research is required. Magnesium alloys have been known to corrode in bone, depending on the manufacturing procedure used to make the magnesium implantation and the alloying ingredients utilised. Magnesium implants were completely corroded, and new bone grew in its place. Rare earth and alloys of magnesium have been found as implant materials that corrode slowly [170]. In bone containing rapidly corroding magnesium alloys, no gas cavities were found, although they were present in nearby soft tissue and subcutaneously. With today's slow-corroding magnesium alloys incorporating rare earth elements, these gas holes are no longer visible [171].

6. RESULTS AND DISCUSSIONS

The research papers examined the use of zinc and its alloys in various biomedical fields, including orthopedics. Zinc-based biomaterials, such as magnesium-manganese-zinc, magnesium-zinc, and magnesium-calcium-zinc, were investigated, along with the incorporation of zinc into calcium phosphate materials. Zinc oxide coatings, bioactive glasses, silver and zinc-doped bio ceramic layers, zinc-based implant materials, and biodegradable metallic wires were also investigated. The studies found that zinc and its alloys have antimicrobial activity, biocompatibility, and controlled breakdown rates, promoting bone development. Zinc also improved osteogenic properties, corrosion resistance, mechanical strength, and biocompatibility of various materials. The study highlighted the potential of zinc and its alloys as drug delivery systems due to their ability to prolong release, target specific cells or tissues, improve drug stability, and increase therapeutic efficacy. Zinc-based materials also showed potential in stent applications, with their ability to inhibit cell proliferation, increase cell adhesion and viability, increase corrosion resistance, and exhibit favorable biocompatibility.

Research studies have shown that tantalum, a biomaterial with superior biocompatibility, corrosion resistance, mechanical properties, and radiopacity, is used in various medical devices such as orthopedic implants, cardiac pacemaker leads, stents, and biosensors. Its adaptability and ability to enhance the performance, dependability, and visibility of medical equipment have been highlighted. Tantalum has also shown promise as a drug delivery medium due to its adaptability, biocompatibility, corrosion resistance, and unique properties. Its mechanical properties, biocompatibility, corrosion resistance, and high purity make it a good material for surgical applications. Tantalum has also been developed for implant applications, such as dental, bone, and tissue implants, and is successfully used in orthopaedics, hernia repair, patellar arthroplasty, spinal surgery, dental implants, and pulp therapy.

Magnesium-based alloys have been used in medical implants since the 19th century, particularly in orthopedic surgery and osteosynthetic procedures. Their mechanical strength, comparable to human cortical bone, has led to their use in bone substitutes, temporary scaffolds, and osteosynthetic plates and screws. Early clinical experiments revealed the impact of corrosion on magnesium implants, leading to gas cavities and complications. However, the use of magnesium alloys improved corrosion resistance and stability, despite challenges like gas cavity formation. The incorporation of rare earth metals marked a turning point in the biodegradable magnesium implant field. The history of magnesium implants reveals a struggle with corrosion-related complications, but the absence of significant harm and observed bone healing despite corrosion have highlighted potential benefits. Researchers have explored alloy compositions with rare earth elements to balance corrosion and biocompatibility, leading to the development of biodegradable stents and orthopedic implants. Current research focuses on refining alloy compositions, manufacturing methods, and surface treatments to optimize corrosion behavior and biocompatibility

7. CONCLUSIONS

The review highlights the unique qualities of tantalum, magnesium, and zinc in biomedical applications. Zinc is ideal for tissue engineering, drug delivery systems, and wound healing due to its antibacterial, biocompatible, and biodegradable properties. On the other hand, tantalum offers exceptional osseointegration, biocompatibility, and mechanical strength, making it ideal for surgical instruments, implants, and bone repair. The choice of material depends on the application conditions and intended results. Tantalum excels in implantology, orthopaedics, and surgical equipment, while zinc shows promise in controlled drug delivery and antibacterial characteristics. Future research should focus on enhancing these materials' properties and investigating novel combinations, surface changes, and production methods. The review provides valuable insights for researchers, physicians, and industry professionals in selecting and developing materials for specific biomedical demands. The progression from corrosion and tissue interaction to the creation of corrosion-resistant alloys may be seen in the history of disposable magnesium implants. Despite initial setbacks, magnesium implants have shown biocompatibility, bone healing promotion, and potential for innovative clinical applications. Rare earth alloys have significantly improved corrosion-related complications. Future collaboration between academia, industry, and hospitals is crucial for developing novel magnesium-based implants for individualized therapies in precision medicine.

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