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Emerging Advanced Materials, Properties for Biomedical Applications

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This paper is a review of recent advances and developments of medically-applicable material systems. The review focuses on three functional clusters of biomedical material systems: synthetic (metals, polymers, ceramics, and composites); naturally derived (animal and plant derived); and semi-synthetic or hybrid materials. These clusters have found various applications in healthcare. The overview highlights significant opportunities and emerging advances for these clusters of biomaterials. This is to aid the development of next generation biocompatible and biodegradable materials for medical applications. This offers scientists, engineers, and technologists tremendous potential to advance know-how in new and improved drug delivery systems, tissue engineering, wound dressing, novel antimicrobial agents, and biosensors for lab-on chip diagnostics. The implications and areas for future research directions are further discussed.

Keywords: Emerging Advanced Materials, Properties, Additive Manufacturing Route, Biomedical Implants and Devices

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1. BACKGROUND TO THE STUDY

Recent advances in biomedical materials systems have and continue to shape the healthcare continuum. From lifesaving stents, drug delivery systems, bone replacement implants, wound irrigation and healing, orthodontics, hearing instruments systems, and countless other applications have benefited from ongoing research and developments efforts. Biomaterials are lifesaving innovations that continue to revamp the continuum of care. Biomedical sciences and engineering have relied on significant advances in material science and engineering over the last forty years (Coulter et al., 2019; Flemings & Cahn, 2000; Hook et al., 2010; Jana et al., 2021; Migliaresi & Nicolais, 1980; Tang et al., 2020; Wegst et al., 2015).

These advances have occurred around composites materials (Migliaresi & Nicolais, 1980), electro-mechanical systems, digital electronics and recently nanotechnology. These advances have been multi-faceted and multidisciplinary.

For instance, advances in as biology, chemistry, robotics, AI, materials science, and engineering (Flemings & Cahn, 2000)(Flemings & Cahn, 2000)(Flemings & Cahn, 2000) continue to inform and revamp adjacent technologies. One of these significant areas of recent advancement is in the field of Nanotechnology, which] promises to further revolutionize the medical and health care spaces. Biomedical materials used in multiple applications are more specialized and offer challenging research opportunities since these materials require a fundamental understanding of in situ properties. Advances in chitosan nanofibers development have opened new routes for scaffolds in neural tissue engineering and regenerative medicine. In vascular and tissue engineering there is the need to employ in treatment, medical scaffolding that are required to be biocompatible, biodegradable, non-immunogenic and support attachment, and proliferation of the cells (S. Li et al., 2014)(S. Li et al., 2014)(S. Li et al., 2014).

As the need to resolve complex clinical challenges continue to evolve, driven by improvement in lifestyles and the overall quality of life, the quest for advance research has been a matter of course (Tang et al., 2020). Our increasing understanding around sustainability has informed the quest for new materials: natural, synthetic, and otherwise. The increasing requirements for low-cost technologies for the developing world is an additional motivation for exploring local and or natural materials as well as augmenting search with functionally engineered materials systems.

The field of biomedical engineering is rapidly evolving. Great strides are being made in the development of novel biomaterials with significant remedy opportunities in disease management. The field of drug delivery has seen advances in microneedles to enhance drug delivery without the pertinent pains associated with traditional needles (Ita, 2015, 2017; McGrath et al., 2014; Prausnitz, 2004; Tuan-Mahmood et al., 2013; Ye et al., 2018; Zhu et al., 2016)(Ita, 2015, 2017; McGrath et al., 2014; Prausnitz, 2004; Tuan-Mahmood et al., 2013; Ye et al., 2018; Zhu et al., 2016)(Ita, 2015, 2017; McGrath et al., 2014; Prausnitz, 2004; Tuan-Mahmood et al., 2013; Ye et al., 2018; Zhu et al., 2016). Stem cell technologies are rapidly advancing and offer potential for improved care across a broad spectrum of diseases and disease management: cardiac, bone-marrow, sickle cell and neurodegenerative (Lunn et al., 2011; Sun & Zhao, 2014) (Lunn et al., 2011; Sun & Zhao, 2014)(Lunn et al., 2011; Sun & Zhao, 2014).

Lab-on-a-chip technology offers the diagnostic regime a new breath of life with the possibilities of point-of-care treatments and low-cost diagnostic systems. Hydrogels and cryogels offer new basis for scaffolds in tissue engineering [1*a)* X. Mao, R. Cheng, H. Zhang, J. Bae, L. Cheng, L. Zhang, L. Deng, W. Cui, Y. Zhang, H. A. Santos, Adv. Sci. 2019, 6, *1801555;*]. Biomaterials are distinguishable from other materials based on its biocompatibility. There have been many definitions for “biocompatibility” but the Food and Drug Administration (FDA) underscores its brevity as a natural or synthetic material that do not cause harm to the human body whether implanted or otherwise. Biomaterials can be clustered into three key functional areas: (a) synthetic (metals, polymers, ceramics, and composites); (b) naturally derived (animal and plant derivatives); (c) semi-synthetic or hybrid materials.

These clusters have found various uses in healthcare. This review highlights recent advances in biomaterials that hold potential in the reconfigurations of medical systems designed to address threats in antibacterial activity, low immunogenicity, wound healing capacity and nascent advances in medical diagnostics. It also delves into recent advances in these clusters and how they would impact the evolving continuum of care.

2. TIMELINES FOR BIOMATERIAL DEVELOPMENT AND CLASSIFICATIONS

Biomaterials are used to design implants or devices. The implants are functional components, which operate without the need for any form of power source. Medical, on the other hand, devices are functional or structural components which require form of chemical or electrical impulses or stimuli to induce some form of energy for them to carry out their intended functions as in mitigation, diagnosis, cure and to capture relevant information for decision-making. These functions are an integral part of the modern care continuum.

The evolution and integration of biomaterials within the modern care space can be categories in four major timelines, which are:

- 1960 – 1970: The first generation of biomaterials were developed and designated as inert biomaterials. The aim of these materials was to replace damaged tissues in the human body while providing the needed structural support with minimal or negligible impact on the overall patient wellbeing.
- 1980 – 1990: These was the decade for the development of bioactive biomaterials (second generation) which are still being used today in various commercial quantities. These were mainly coatings that induce a biological reaction of chemical nature between the patient and the contact area. This is to ensure effectiveness of the medical device and a boost to its intended function in the human body. The drawback of bioactive biomaterials was potential toxicity to the host due to immunological processes occurring simultaneously while the material is in operation.
- 2000 – 2010: These third-generation biomaterials were designed to curb the shortcomings of those of the second-generation. The main aim is for them to be biodegradable – to degrade and be absorbed by the host. These are not necessarily permanent implants and do not require any interventional surgical procedure(s) to correct or to remove them.
- 2010 – date: This is the fourth generation, which are referred to as smart biomaterials. These materials are results of the advances in biotechnology, information technology, materials science, and engineering. These materials are designed and tailored to emulate the natural mechanisms and structures of the human body. They provide conditions for self-repair, self-healing, and the regeneration of damaged tissues through specific reaction of the cell. These classes are also referred to as biomimetic biomaterials, which can be transient devices such as plates, screws, and prostheses. With all the merits associated with this class of biomaterials, they are yet to experience widespread usage.

Although four evolutions have taken place in the design of biomaterials, the first generation are commonly and widely used. The major classes of biomaterials based on material classification, applications and characteristics are given in **Error! Reference source not found.**. However, there are various classes of biomaterials described. The critical factor that determines the choice of use of a particular class of material is mechanical behaviour, natural properties, biocompatibility, and material degradation resulting from corrosion. Other significant considerations include cost, processing routes, availability and in-service performance. Some of the major areas for biomaterial applications are given in

Table 1.

Table 1: Some Major areas of biomaterial applications

Care of application	Examples of medical devices and implants applicable
Catheters and drug delivery controlling devices	Coating for capsules and tablets, transdermal systems, microcapsules, and implants
Diagnostics	Stretchable and wearable device for human organ monitoring
Dental implants	Tooth replacements
Extracorporeal	Dialyzers, oxygenators, and plasmapheresis
General surgery	Adhesives, blood substitutes, sutures, and staples
Neural implants	Cochlear implants and hydrocephalus shunt
Plastic and reconstructive implants	Augmentation or reconstruction of breast, penile implant, and maxillofacial reconstruction
Cardiovascular implants	Stents, heart, valves, pacemakers, and vascular grafts
Ophthalmic systems	Contact and intraocular lenses
Orthopedic protheses	Hip joint, knee joints and fracture fixation

3. SYNTHETIC MATERIALS (METALS, POLYMERS, CERAMICS, AND COMPOSITES)

Biomaterials are based on the different classes of synthetic materials. These include metals, polymers, ceramics, and composites. Some of the constituent elements used for the design of these materials are active components and ingredients of the human body. Some of these macro and trace elements and their roles in the human body is given in

Table 2 Error! Reference source not found..

Table 2: Major and Trace Elements In The Human Body And Their Benefits.

Macro elements	Benefits and roles
Ca	Instrumental in the formation of bones and teeth
P	Instrumental in the formation of bones and teeth. Responsible for the energy carrier in animals
O, C, H and N	Forms the molecular structure of proteins and active component of water in the body
Mg	Sufficient for bone formation and deficiency could lead to muscle spasms or tetany
Na, K and Cl	The main electrolyte for extracellular fluids and the blood. Critical for maintaining osmotic balance and pH of the body
S	Critical to detox the body and mainly in biotin and thiamin
Trace elements	**Benefits and roles**
Fe	Transportation of oxygen in blood cells and essential for the formation of hemoglobin molecules in the blood and myoglobin molecules in the molecules
Cu	Essential for iron metabolism and it has anti-inflammatory, anti-infectious properties.
Mn	Necessary for the production of heathy bones and collagen which is used in wound healing

I	Essential for metabolism and thyroxine
Zn	Essential for procreation and DNA binding
Co	In Vitamin B12 and excess causes cardiac failure
Mo	Excretion of N in uric acids and deficiency causes diarrhea
Cr	Regulate sugar levels and deficiency causes hyperglycemia

There are merits and demerits to the use of biomaterials. Table 3 gives an overview of the general characteristics of these materials, which are mainly good mechanical properties, biocompatibility, ease of fabrication and corrosion resistance. The chemical nature of most of these materials results in complications with dissolution into the bloodstream.

Table 3: General Characteristics, Merits, Demerits, And Potential Applications Of The Main Classes Of Biomaterials.

Classes of materials	Merits	Demerits	Potential applications	Refs
Metallic materials	Great mechanical properties (tensile strength, fatigue strength, fracture toughness) Easy to fabricate, Easy to sterilize, Biocompatible	Generally corrosive High elastic modulus Aseptic loosening Low biocompatibility with some grades	Orthopedics implants, dental implants, pins, staples, joint protheses, cranial plaques screws, plates, and guiding wires	(Hussein et al., 2015; S. Li et al., 2014)(Hussein et al., 2015; S. Li et al., 2014)
Polymeric materials	Biocompatible, Biodegradable Easily available, Workable mechanical properties (strength)	Can leach easily into body fluids Difficult to sterilize Poor mechanical property	Drug delivery systems, dental implants, scaffolds for tissue engineering, sutures, prostheses, orthopedics implants, arteries, artificial tendons and adhesives in dentistry	(S. Li et al., 2014)(S. Li et al., 2014)
Ceramics materials	Tailorable mechanical properties, Biocompatible Corrosion resistant	High elastic modulus Difficult to manufacture	Cochlear implants, dental parts, coatings, bone filling, medical equipment and tools	(S. Li et al., 2014), (S. Li et al., 2014)
Composite materials	Good mechanical properties, Corrosion resistant, Biocompatible	Expensive, Difficult to fabricate	Porous orthopedic implants rubber catheters and gloves Dental fillings, heart valves	(S. Li et al., 2014),(S. Li et al., 2014)

			Implants and artificial joints	

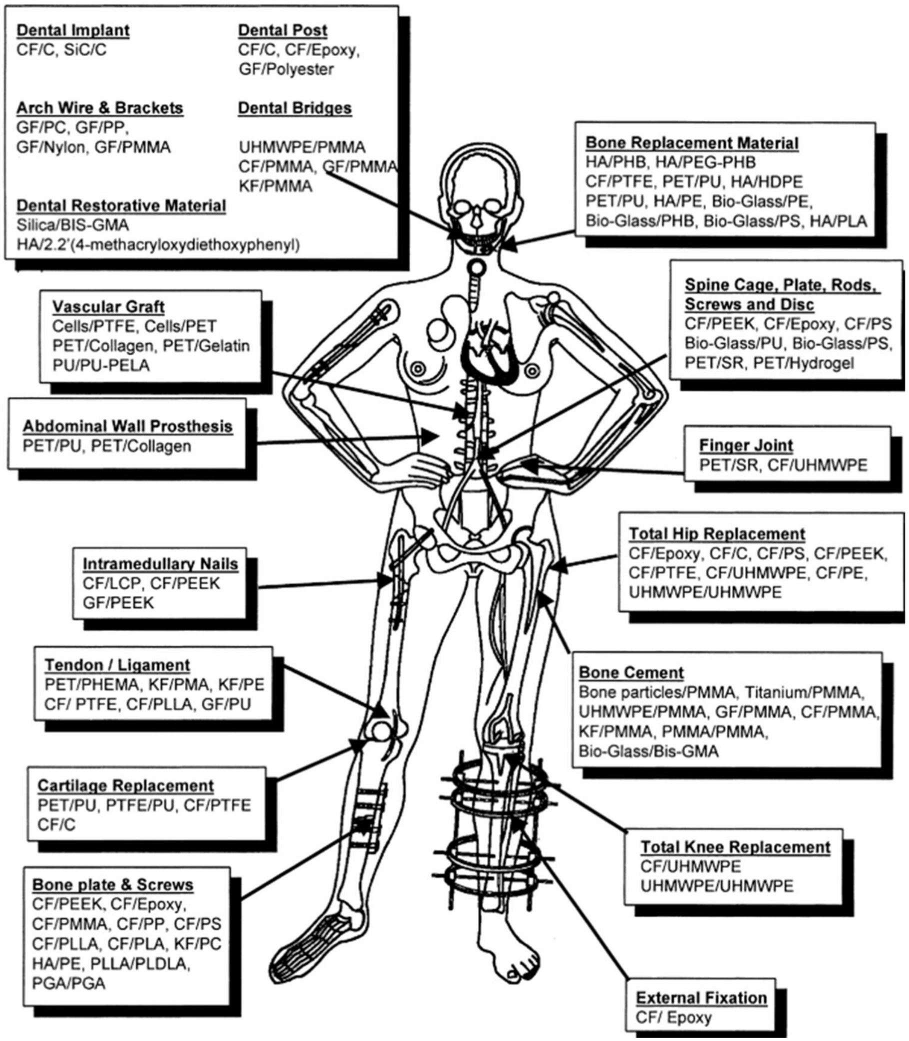

Figure 1: Schematic Diagram Of The Human Anatomy With Accompanying Biomaterial With Replacement Potential

Abbreviations:
C – carbon, CF – Carbon Fibers, GF – glass fibers, KF – Kevlar fibers, PMMA – polymethylmethacrylate, PS – Polysulfone, PP – Polypropylene, UHMWPE – ultra-high molecular weight polyethylene, PLDLA – Poly (L-DL- lactide), PLLA – poly(L-lactic acid), PGA – Polyglycolic acid, PC – Polycarbonate, PEEK – polyethyleneretherketone, HA – Hydroxyyapatite, PMA: polymethylacrylate, BIS-GMA: bis-phenol A glycidyl methacrylate, PU: polyurethane, PTFE: Polytetrafluoroethylene, PET: polyethyleneterephthalate, PEA: polytethylacrylate, SR: Silicone rubber, PELA: Block polymer of lactic acid and polyethylene glycol, LCP: Liquid crystalline polymer, PhB: Polyhydroxybutyrate, PEG: Polyethyleneglycol, PHEMA: Poly(20hydroxyethyl methacrylate) (Ramakrishna et al., 2001).

3.1. Metallic biomaterials

Globally, metallic biomaterials account for ~70 – 80% of implants. This is mainly attributed to excellent mechanical, physical, and chemical properties. Some of the first metallic materials used for biomedical applications were stainless steel and Cr-Co alloys [ ]. Ti-based alloys were introduced in the 40s and the Ti-Ni alloys in the 60s. One of the first of the Ti-Ni alloy was the nitinol (equiatomic composition of Ti and Ni).

Metal prosthetics have supported the physically challenged in multiple ways. They have found effective uses as straighteners, clutches, walkers, wheelchairs, surgical tools, guiding wire and implants. Titanium hipbones, knee caps, screws, braces, and toes have been an integral part of the emerging biotechnology landscape. The mechanical properties of the predominantly used metallic biomaterials and how they compare to human bones is given in Table 3 Error! Reference source not found. (Ramakrishna et al., 2001).

Table 3 Properties of Typical Metals For Biomedical Applications (Sumitomo et al., 2002)

Metal	E (GPa)	ρ (g/cm3)	YS (MPa)	UTS (MPa
Co – Cr alloys	220 – 230	~8	275 – 1585	600 – 1785
Ti-based	105 – 125	~4.5	840 -1100	590 -1024
Stainless steels	205 – 210	~8.4	170 – 750	465 – 950
Mg-based	45	~1.7	165 – 275	280 - 365
Cortical bone	10 – 30	1 – 2	45 – 55	45 - 50

The main factors relevant for the design of metallic biomaterials are as follows:

- Excellent and non-toxic biocompatibility
- Great corrosion resistance behaviour
- Great mechanical properties comparable to the type of implant or non-implants
- Great wear resistance behaviour
- The need for Osseo-integration for bone prosthetics

3.1.1. Titanium-based Alloys

Titanium and Ti-based alloys have been extensively used for biomedical applications. The various grades of pure Ti and Ti-based alloys are given in Table 4. These biomaterials are generally classified as a, b and a+b grades. Pure Ti grades fall under the a grade, whereas alloyed Ti-based materials fall under b and a+b grades. The a-Ti contains impurities like iron and oxygen which increases strength and hardness through solid solution hardening (Mauritz, 2012). These alloys have been used as brace for teeth straightening, screws for tooth replacement and complex surgical guides. In some instance, titanium surfaces are shot peened to enhance both bone growth and adhesion(Bammidi et al., 2020). Bone recession has been a major drawback and continues to require intensive medical and engineering considerations.

The resilience, durability, and biocompatible of titanium has been its greatest biomedical consideration albeit cost. Titanium kneecaps are known for their anti-wear and robustness. Structural integrity of implants is one of the most important considerations which Ti-based alloys possess. The superior mechanical property of T-based alloys compared to other metallic biomaterials contribute to their increased usage as implants. It withstands most stress systems in the body and is biostable (Valiev et al, 2008) The advent of printable titanium parts especially for aerospace and medical consideration brings titanium applications to a new level. Such printable are known for lightness, toughness, considerable strength, durability and biocompatible.

Table 4: Typical Ti-based biomaterials with relevant mechanical properties (Mitsuo, 1998).

Alloy	Type	S_y (MPa)	UTS (MPa)	Reduction in area (%)	Elongation (%)	E (GPa)
Grade 1 (Pure Ti)		170	~240	~30	24	102.7
Grade 2 (Pure Ti)		275	345		20	
Grade 3 (Pure Ti		380	450		18	103.4
Grade 4 (Pure Ti)		485	550	25	15	104.1
Ti-13Nb-13Zr (aged)	b	836-908	973 - 1037	27 - 53	10-16	79 - 84
Tiadyne 1610 (aged)		736	851	-	10	81
Ti-12Mo-6Zr-2Fe (annealed)		1060	1060 - 1100	64 - 73	18 - 22	74 - 85
Ti-15Mo (annealed)		544	874	82	21	78
Ti-15Mo-5Zr-3Al (aged)		1000 - 1060	1060 - 1100	64 - 73	18 - 22	-
Ti-15Mo-5Zr-3Al (ST)		838	852	48	25	80
Ti-15Mo-2.8Nb-0.2Si (annealed)		945 - 987	979 - 999	60	16 - 18	83
Ti-35.3Nb-13Ta-7.1Zr		547.1	596.7	68	19	55
Ti-29Nb-13Ta-4.6Zr (aged)		864	911		13	80
Ti-6Al-4V (annealed)	a+b	825 - 869	895 - 930	20 - 25	6 - 10	110 - 114
Ti-6Al-4V (Mill & annealed)		795 - 875	860 - 965	25 - 47	10 -15	101 - 110
Ti-5Al-2.5Fe		895	1020	35	15	112
Ti-6Al-7Nb		880 - 950	900 - 1050	25 - 45	8 - 15	114
Ti-5Al-1.5B		820 - 930	925 - 1080	36 - 45	15 - 17	110
Ti-15Sn-4Nb-2Ta-0.2Pd (aged)		1020	1109	39	10	103
Ti-15Sn-4Nb-2Ta-0.2Pd (annealed)		790	860	64	21	89
Ti-15Zr-4Nb-4Ta-0.2Pd (aged)		806	919	72	18	99
Ti-15Zr-4Nb-4Ta-0.2Pd (annealed)		693	715	67	28	94

3.1.2. Chromium – Cobalt Based Alloys

The Cr-Co based alloys were developed specially for aerospace applications in the 1900s by Haynes (Festas et al., 2020)(Festas et al., 2020). These alloys were applied at sections of the aircraft engine but was adapted as a biomaterial due to being bioinert. The derivative of the alloys has nominal compositions as ~60.6% Co, ~31.5%Cr and ~6% Mo, and was proposed in 1932 for medical components (Markatos et al., 2016)(Markatos et al., 2016). The Cr-Co based alloys are not magnetic, high corrosion- and wear-resistant and are widely used as artificial joints, dental and orthopedic implants (arthroplasty) (Festas et al., 2020; Jay, 2016; Markatos et al., 2016)(Festas et al., 2020; Jay, 2016; Markatos et al., 2016). They are durable and suitable for long-term implants. The drawback of these alloys is the difficulty in machining, which is attributable to the relatively high hardness and associated increase manufacturing cost. To ensure efficient cutting, the parameters need to be optimized significantly.

Based on the ASTM standards, four classes of Cr-Co based alloys are suitable for various biomedical applications. The mechanical properties of these classes are given in Table 5. The elastic modulus is higher than cortical bones and most Ti-based alloys with high density and stiffness. This causes higher stress shielding compared to most Ti-based and Mg alloys. Osseointegration and biocompatibility behaviour of Co-Cr based alloys are lower than in Ti-based alloys. Thus, Co-Cr based alloys are used for applications that do not require interaction with the bones. This spinal fixation rods but leads to mechanically assisted crevice corrosion with site between the Ti and Co-Cr shredded. This leads to metallosis, when used in total hip arthroplasty (Prasad et al., 2017).

Table 5: Mechanical properties of standard Cr-Co based biomaterials according to the ASTM standard (Chen & Thouas, 2015).

Metal	E (GPa)	ρ (g/cm3)	YS (MPa)	UTS (MPa
F75 (Co-Cr-Mo)	210	15	650 – 890	450 – 520
F90 (Co-20Cr-15W-10Ni)	210	-	950 – 1120	450 – 650
F562 (Co-35Ni-20Cr-10Mo)	230	8	790 – 1000	960 – 1000
F1537 (Co-28Cr-6Mo)	220	13 – 23	580 – 930	1020 – 1360

The compositions of the Cr-Co based alloys have better corrosion resistance compared to stainless steels. The Cr contents contribute to the formation of the Cr-oxide passive layer. The effects of the main alloying elements in the Cr-Co based alloys are given in Table 6. These alloying elements contribute significantly to the mechanical, physical and corrosion properties by modifying relevant microstructural features.

Table 6: Role of alloying element on mechanical and corrosion properties (Chen & Thouas, 2015; Ibrahim et al., 2017).

Elements	Effect on mechanical, physical and corrosion properties
Cr	Improve wear and corrosion resistance. It forms stable passive layers which are chrome carbides ($Cr_{23}C_6$).
Mo	Contributes to solid-solution strengthening, refines the grain sizes and improves corrosion resistance.
Ni	Increase the castability, solid solution strengthening enhancement and increases corrosion resistance. Nickel is potentially toxic
C	Increase the casting behaviour and contribute to wear resistance by enhancing the strength and hardness while forming chrome carbides ($Cr_{23}C_6$).
W	Decrease corrosion resistance, enhance solid-solution strengthening, reduces shrinkage cavity, gas blow holes and segregation at the grain boundaries

The number of successful total hip replacement surgery is projected to increase from 200 000 in 2003 to 572 000 by 2030 (Kurtz et al., 2007)(Kurtz et al., 2007). The bearing surfaces of most artificial hip replacements are produced from Cr-Mo and Cr-Co-Mo alloys. Other materials that could perform the same function are the ultra-high molecular weight polyethylene (UHMWPE), alumina and oxygen diffusion hardened ZrNb alloys). Generally, for metal-on-polyethylene (MoP) arthroplasty, Cr-Co-Mo femoral ball is used, whereas the cup is made from UHMWPE material (Liao et al., 2013)(Liao et al., 2013).The Cr-Co-Mo alloys are ideal for long-term implants. Generally, Cr-Co based alloys have excellent corrosion resistance, hence a great candidate for total joint replacements. It was one of the first alloys used as stem material in total hip replacement in 1950 due to its high strength and high ductility. About 20% of total hip replacement implants are made of hard-on-hard bearing system or stems from wrought CoCrMo alloys.

These alloys are also used for fracture-fixation but not common because they are expensive compared to stainless steels. The Cr-Co alloys have been explored for coronary stents (Garg & Serruys, 2010; Kereiakes et al., 2003)(Garg & Serruys, 2010; Kereiakes et al., 2003) and for auxetic meta-biomaterial for bone scaffolds and implant (Wanniarachchi et al., 2022)(Wanniarachchi et al., 2022).

3.1.3. Magnesium-Based Alloys

Magnesium is an essential element in human bones and is very benign. Elemental Mg in humans form non-toxic soluble products excreted innocuously through urine. The yield and tensile strength of Ti-based, W-based, and stainless-steel biomaterials are relatively higher than a typical bone in the human body. The high strength and high elastic modulus of these materials when used as implants contribute to stress-shielding near neighboring tissues (Ramalingam et al., 2020). Thus, there is the need for biomaterials with strength within the domain of human bones to reduce any excessive stress induced discomfort. The Mg-based materials are ideal substitute biomaterials.

In recent advances in biological applications, biodegradable materials allow implants to gradually degrade and aid the healing process without a second surgery to remove them. Magnesium and its alloys forms on the three subgroups of biodegradable materials (H. Li et al., 2014; Qin et al., 2019). Mg has similar properties to bone in addition to its biocompatibility, thus very suitable biodegradable material. Rapid degradation of Mg at the initial stage of implants affects mechanical integrity leading to failure before healing process. Alloying with other materials and surface coating helps reduce the corrosion rate which is the main disadvantage of Mg and its alloys (Banerjee et al., 2019; Hornberger et al., 2012)

3.1.4. Shape memory alloys

Shape Memory Alloys (SMAs) are metallic alloys that revert to original form when subjected to a memorization process between two transformation phases. These process are temperature or magnetic field dependent through a phenomenon known as shape memory effect (SME) (Mohammadi, 2012). Nickel-titanium (NiTi) alloy exhibit SME and is used for biomedical applications (Morgan, 2004; Pelton et al., 2000; Stoeckel, 2000; T. et al., 1999; Tarniță et al., 2008) such as orthodontic arch wires, guidewires, stents, dental drills, catheter tubes, ASD patches (Stoeckel, 2000). The properties of SMA that makes them suitable for medical applications include the following (T. et al., 1999): elastic deployment, thermal deployment, kink resistance, constant stress, dynamic interference, stress hysteresis, and temperature dependence of stress.

For engineering and commercial applications, thermo-responsive SMA has seen increased applications. Among the three major groups of SMA currently in use, NiTi-based and Cu based are more suitable for engineering applications, while Fe-based is seldomly used (Duerig et al., 2012). Advanced technologies (laser cutting and waterjet) have been developed for handling NiTi alloys because of the difficulty in machining these with conventional techniques(Huang et al., 2002; Pfeifer et al., 2010; Xie et al., 2003).

Table 7 shows a summary of the mechanical properties of different metallic materials used for porous scaffolds.

Table 7: Summary of the mechanical properties of different metallic materials used for porous scaffolds.

Materials and their structure	Elastic modulus (GPa)	Yield strength (MPa)	References
Ti-6Al-4V (Gyroid and Diamond	3.8	145.7 – 152.6	
Ti-6Al-4V (Octahedral)	2.1 – 4.7	71 – 190	
Pure Ti (Diamond)	0.557 – 0.661	50	
Pure Ti (FGPS)	0.28 – 0.59	3.79 – 17.75	
Pure Ta (Diamond)	3.1	393.62	
Pure Ta (Dodecahedron)	1.22	12.7	
Ti30Nb-5Ta-8Zr (Rhombic dodecahedron)	0.7 – 4.4	12.6 – 67	
Ti35Zr28Nb (FCC)	1.1	27	
Ti35Nb2Ta3Zr	3.1 – 3.9	136 – 149	
CoCr F75 (Diamond)	2.22 -3.43	75.89 – 116.34	
NiTi (Octahedron, cellular gyroid, sheet gyroid)	-	21 - 44	
NiTi	3.7 -13.5	-	
316L (gyroid)	2.04 – 2.71	55 – 89.4	
316L (gyroid)	14.41 – 15.53	251 – 302	
Fe (Diamond)	0.89 – 2.81	10.7 – 53.1	
Fe-35Mn (Schwarz Primitive	33.5	304	
Zn (Diamond)	0.786	10.8	
Mg WE43 (Diamond)	0.7 – 0.8	23	

3.2. Polymeric Biomaterials

Polymeric biomaterials are finding useful application in the biomedical device spaces. Infact, one of the first polymeric materials used as biomaterials is the methyl methacrylate resin. Initial applications were not successful until it was used as a tooth replica implant in the late 1960s. Polymeric biomaterials are being used extensively in regenerative medicine and tissue engineering scaffolds (Bhat & Kumar, 2012; Nair & Laurencin, 2007; Yin & Yang, 2020). Commercial examples are polyethylene (PE), silicone rubber, poly vinyl chloride, poly methyl methacrylate, polyethylene terephthalate and poly tetrafluoroethylene. Similarly, some of the materials are also being used for oral vaccination and drug delivery (Jana et al., 2021).

The success application of these classes of materials is driven by the very low or near zero toxicity, highly biodegradable (Agarwal, 2020) and very biocompatible (histocompatibility and hemocompatibility) without an adverse effect of inflammatory response (Walia et al., 2020) and immunological rejections (Gao et al., 2021) with organs and tissues in humans (Bhat & Kumar, 2012; Jana et al., 2021; Nair & Laurencin, 2007).
Polymers became useful biomaterials due to the following properties and qualities (Teo et al., 2016):

- Ease of fabrication and reproducibility due of altering compositions.
- Polymers do not generate magnetic or electric charges as in metallic materials
- Easy to be characterized mechanically and microstructurally
- The connective tissue attachment is fibrous with aesthetic qualities

There are some drawbacks associated with polymers. These include poor adhesive to living tissues, poor mechanical properties, and susceptibility to adverse immunological reactions. The two types of polymeric biomaterials are natural and synthetic. The natural polymers are poly(amino acids), polysaccharides, protein and protein-based, whereas synthetic polymers range from aliphatic polyesters, nylons, polyurethanes, polymethylmethacrylate, polytetrafluorethylene (Teflon).
Table 8 shows the natural and synthetic polymers and their various functional biomedical applications.

Table 8: Summary of the properties of natural and synthetic polymeric materials with various functional applications as medical implants and devices.

Classes of polymers as biomaterials	
Natural polymers	**General remarks and functional applications**
Protein-based polymer	Biocompatible, non-toxic, absorbable, and used in tissue engineering and implants
Albumin	Cell and micro-scale drug encapsulation
Collagen	Wound dressing, drug delivery microsphere system and absorbable sutures
Polyaminoacids	Non-toxic, biocompatible, non-antigenic and for oligomeric drug carriers. Examples are poly (aspartic acid), poly (α, L-Lysine) and poly (α, L-glutamic acid)
Polysaccharides and their derivatives – flora-based sources	
Agarose	Used as supporting material in clinical analysis and for immobilization matrix
Alignate (marine and algae)	Superior gel-formation properties, biocompatible with viscosity and microstructural properties dependent on composition. Use for immobilization for enzymes and cells. For controlled release of bioactive substances as well as injectable capsules for the treatment of hormone-deficient and neurodegenerative diseases.
Carboxymethyl cellulose	Immobilization of cells by combining polyelectrolyte complex formation and ionotropic gelation with chitosan for applications in drug delivery systems and dialysis membranes

Carrageenan	Thermo-reversible properties are excellent and use for micro-scale encapsulation
Cellulose sulphate	Part of polyelectrolyte complexes for immunoisolation, complex-forming ability highly sensitive to acylation
Polysaccharides and their derivatives – Human and fauna-based sources	
Sources from Human and fauna	
Heparin-like glycosaminoglycanes	Anticoagulant and antithrombotic properties. Applied extensively in surgical operations. Some are good for capsule formation and ionotropic gelation.
Hyaluronic acid	Excellent therapeutic agent and great lubricant
Polysaccharides through microbial action	
Chitosan and derivatives	Non-toxic, biocompatible, natural polycation, excellent film- and gel- forming capabilities. Used for controlled-delivery systems in gels, microspheres, and membranes.
Dextran and derivatives	Superb rheological properties, plasma expander and suitable as drug carrier
Synthetic polymers	
Nylons (Polyamides)	Applied as sutures, hemofiltration membranes and dressing
Thermoplastic polyurethanes	Great elastomeric properties and for permanent implants (vascular grafts and protheses), drug delivery systems and catheters. Current applications for artificial heart still being investigated.
Polyphosphazenes	Tailorable with side-chain functionality. Can be organized into hydrogels and films, and for application in areas of drug delivery
Polyanhydrides	Applied in tissue engineering, biodegradable and active for releasing bioactive molecules into the body
Low density polyethylene	In surgical operations as membranes, sutures, and catheters.
Poly (ortho esters)	Surface-eroding macromolecules and used for sustained dry delivery systems and for ophthalmology.
Poly (cyanoacrylates)	Biodegradable but dependent on the alkyl chains. Use as surgical glues and adhesives with prospect for drug delivery
Polyethylene oxide	Superb biocompatibility and applicable to variety of biomedical applications
Poly vinyl alcohol	Blended membranes and gels for cell immunoisolation and drug delivery systems
Poly hydroxyethyl methacrylate	Hydrogels for soft contact lenses, drug delivery systems, skin coatings and cell immunoisolation membranes
Polytetrafluoroethylene (Teflon)	Vascular grafts, coatings, sutures and clips
Polymethyl methacrylate (PMMA)	Dental implants and bone replacements. Combined easily with other copolymers
Polydimethylsiloxanes	Implant for orthopedic and plastic surgery. Blood bags and pacemakers
Aliphatic polyesters	

Poly glycolic acid), poly (lactic acid) and their copolymers	Applied in tissue engineering, drug delivery systems and sutures. Biodegradable and easily copolymerized for regulation of degradation time
Poly hydroxy butyrate, poly alkylene succinates	Biodegradable, a potent matrix for drug delivery systems, cell microencapsulation. Mechanical properties can be changed by copolymerization, modification of composition and blending.
Environmentally responsive synthetic polymers	
Poly vinyl methyl ether	Non-toxic, sensitive to changes in temperature and superb shape memory effects
Poly N-alkylacrylamides	Gels sensitive to temperature changes and critical low temperatures adjustable with incorporation of co-monomer
Polyethylene oxide – b – propylene oxide	Surfactant with amphiphilic properties. Used for skin treatment and protein delivery

Some of the polymers have been used for bone cement for orthopedic applications (poly methyl methacrylate), bone screws, dental implants (poly vinyl siloxane), soft contact lenses (poly hydroxyethyl methacrylate), surgical sutures (poly glycolic acids) and hernia repairs (polypropylene). Some of the common polymeric materials and their characteristic behaviors are given in Table 9.

Table 9: Characteristics mechanical, physical, and chemical behaviour of polymeric biomaterials.

Polymeric materials	Advantages	Disadvantages
Polyethylene	Excellent chemical resistance, modification of mechanical properties based on molecular weight, low melting point, lightweight, biocompatible, good elasticity and great anti-infective properties and quick drying and curing characteristics	High friction coefficient, Poor ability to dye and “plastic feel” to the skin
Polypropylene	Non-toxic, High melting point, good dielectric properties, In the form of homopolymer and copolymer with diverse mechanical properties	Non-degradable, not fully biocompatible, Semi rigid material causing local discomfort
PVDF	Bio and chemically inert, great strength and stiffness, Strong piezoelectric effect, good biocompatibility and good resistance to hydrolysis	Difficult to form smooth films, Low thermal stability, Poor adhesion properties
PMMA	Good mechanical properties, lightweight, Poor electrical and thermal conductivity, Radiolucency and acceptable biocompatibility	High curing temperature and Poor to osseointegration
Polyurethane	Durability is high, toughness is great, good hemocompatibility and biocompatibility, good biostability, low coefficient of	Environmentally induced stress cracking, Metal ion oxidation and In vivo material degradation

	friction and low water permeability	
Silicone	Bio and chemically inert, Low toxicity, good biocompatibility, low thermal conductivity, Thermal stability, high gas permeability and Hydrophobic	Long-term effects on studied, high coefficient of friction, prong to damage during implantation due to softening, Size and swelling effects, Propensity for protein absorption and Low life expectancy
Polytetrafluorethylene	Bio and chemical inert, mechanically durable and strong, Hydrophobic and Electrically inert	Very stiff, susceptible to damage from traction when lead migrates, has insulation microdefects
Polymeric materials	Advantages	Disadvantages
Polyimide	good chemical resistance, good electrical and mechanical properties, Low creep properties, High tensile strength, Flexible and can be folded into compact module, Stable over wide range of temperature, High heat resistance, High light transmittance for a wide wavelength and some biocompatible when reacted with blood	High moisture absorption
Polyamide (nylon)	Minimal tissue reactivity, Long-lasting high elasticity and tensile strength, High and varying electrical properties, Moisture absorbent and Able to prevent bacterial transmission	Moisture permeability, poor heat sealability and High friction coefficient
Liquid crystal polymer	Bio and chemically inert, Fire resistance, Low moisture absorption, Able to fabricate thin layers, Good MRI capability, High durability and mechanical strength	Composite film has poor adhesion to flexible substrates
CNT	Insulative and electrically conductive in specified orientation, mechanically strong with high elastic modulus and tensile modulus, good bonding strength with metal substrates with good packing density	Cytotoxicity, Weak against shearing between adjacent shells and easily compressed because of their hollow structure

Poly (lactic acid) (PLA), poly (glycolic acid) (PGA), and poly (lactic-co-glycolic acid) (PLGA) are a group of (α-hydroxy acids) synthetic biopolymers that are most widely used and has been extensively studied (Budak et al., 2020). PGA has a high production cost on a large scale, and it often referred to as a precious biopolymer. PGA is used for biomedical applications such as barrier membranes, stents, sutures, tissue engineering, drug delivery, dental, and dental applications.

Its use for medical applications is due to its biocompatibility, mechanical strength, and biodegradable characteristics. Polylactic acid (PLA) is a biopolymer which is bioabsorbable and biocompatible, thus used as biomaterial in medical fields like orthopedics and oral surgery (Mohanty et al., 2000; Takayama, 2006. Tg of –60VC and a low Tm of 60VC. At room temperature, PCL is tough and semi-rigid. tough and semi-rigid.

7. CONCLUDING REMARKS FUTURE WORKS

The biomaterial research space has gained significant impetus in the last two decades and continues to show great promise. In this paper, we reviewed several biomaterials and discussed cogent properties that made them materials for biomedical artifacts. Generally, the Mg has low density and lightweight but with inferior corrosion and wear resistance. Titanium-based alloys, especially Ti6Al4V is the most widely used metallic biomaterial due to excellent corrosion resistance and great osseointegration than for most stainless-steel grades. In the case of CoCrMo, they are biocompatible with promising mechanical properties such as high elastic modulus and strength. These alloys also have good strength, corrosion, fatigue, and wear resistance.

Our future research will further explore Hydrogels and cryogels as biomaterials, graphitic carbon nitride-based materials, Ceramic biomaterials, Composite biomaterials, Complex concentrated alloys for biomedical application, Naturally-derived (animal and plant) biomaterials, Collagen-based biomaterials, Chitin and Chitosan nanofibrous materials, Semi-synthetic or hybrid materials.

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