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Review Article

A Survey on Additively Manufactured Nanocomposite Biomaterial for Orthopaedic Applications

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The sturdy demands in orthopaedics are not yet fulfilled, in both bone replacement and joint substitution and also in other repairs of bone defects. Metals are used for bone repair and replacement for a long period of time instead of biomaterial. Most of the countries are still now practising bone replacement with metals like titanium and stainless steel only due to the lag of technology advancement. A lot of research and development paves the way to composite biomaterial, as it is evolving in the domain of treatment of orthopaedics. There was massive research undergoing in the biomaterial field recently, and various methods of fabrication have been tested and implemented. Nanocomposites provide a higher surface-to-volume ratio, surface chemistry and nanoscale reinforcement, flexible production techniques, good corrosion and erosion resistance, and cheaper costs. The nanocomposite biomaterials were intended for biomedical purposes. Because of the intricacy of biological structures (tissue or organ) and additive manufacturing techniques for tissue engineering, scaffolding has wide scope for instant remedies in bone implant. The design restrictions and physical attributes of fast prototyping structures are then evaluated in terms of input factors like design elements, material choices, and additive manufacturing processing parameters. As a result of this survey, the needs and application importance of additively manufactured implants for the regeneration of various biomaterial types as well as the attempts undertaken to mitigate their medical impairment are suggested.

1. Introduction

In the last three years, the number of new fracture cases worldwide is expected to reach 17.8 crore, 33.4 percent from 1990. Males were responsible for 30.2 crore new fracture cases, while females were responsible for 21.64 crore new fracture cases. There were 6.6 thousand age-standardised fracture cases per one lakh persons. With 7.6 incidents per one lakh inhabitants, men had a higher age-standardised rate than females. Ladies had a 57.4 percent greater incidence rate than men in the population aged 95 and up. In all age categories, 60-year-old men had more fracture incidence rates than females, despite having higher fracture incidence rates in age-standardised and fracture incidence rates as per the all age group. A bone transplant was required for these patients. Despite the fact that both autogenous and allogenous bone have disadvantages such as donor scarcity and infection risk, both have been routinely employed for bone graft-based therapies. Alternatives to synthetic and natural biomaterials have been discovered, and a number of these are now commercially accessible for bone transplantation, creating a synthetic graft that can mimic bone tissue in appearance while modifying the needed function in osteoblast and progenitor cell populations. However, it remains a significant difficulty.

The nanocomposite structure of natural bone tissue provides adequate physical and biological qualities. The biomaterial used to create bone tissue must be as near to genuine bone tissue as possible. They are important in the regeneration of bone tissue because they have a combination of beneficial biological features, appropriate matrix environment, since no one substance is capable of reproducing the mixture, structure, and characteristics of natural bone; and enable regulated; for bone graft substitutes at various phases, several growth agents are distributed sequentially. The formulation, texture, and sophisticated nanocomposites for osteocollagen synthesis features are discussed in this article. The researchers looked at biomimetic manufacturing of osteoclast nanocomposites and facilitated healing utilising harmless biomaterials and biologically active nanostructured composite materials and nanocomposite scaffolds for bone graft substitutes. The synthesis, design, and characterisation of such nanocomposites in vitro and in vivo are discussed.

1.1. Metallic Biomaterials for Additive Manufacturing. The recruitment of mesenchymal stem and pluripotent osteoprogenitor cells to a fracture healing site is known as osteoinduction. As a result, they should be encouraged to join the osteogenic transition process. When the amount of bone that has to be replaced is enormous, organic osteoinduction paired with a biodegradable scaffold may not be adequate. As a result, the scaffold will encourage bone development by being osteoinductive. When a large volume of bone needs to be replaced, natural osteoinduction combined with a biodegradable scaffold may not be adequate. As a result, the scaffold should promote bone growth by becoming osteoinductive [1].

In the realm of orthopaedics, metal nanocomposite materials have lately garnered basic investigation. Magnesium (Mg), for example, is well-known for its great biocompatibility and mechanical characteristics that are identical to those of real bone [2]. As a result, it is preferred over conventional metallic materials in orthopaedic implants. However, the "Mg" application in this field is limited by two significant drawbacks: early degradation and low bioactivity. Nano-HA and nano-TiO_2 have recently been reported as reinforcing materials in Mg matrix. MgO-coated Mg-HA-TiO_2 nanocomposite greatly increased the modulus and resistance to oxidation of Mg-based nanocomposite [3]. Compared to ceramics and polymers, studies show that ceramic-polymer nanocomposites are more successful for repair of articular cartilage due to improved mechanical characteristics and bioactivity. Articular cartilage is the white smooth tissue that surrounds the ends of bones where they connect to create joints [4].

Metal alloys of extensive variety have been incorporated into additive manufacturing systems, especially on the laser-powder bed fusion technique (L-PBF). The latest advances in L-PBF include printing high-density parts (99.5%) using the selective laser melting (SLM) process, which is also known as direct metal laser sintering (DMLS) [5]. The most common metallic biomaterials (i.e., scaffolds) printed using the laser powder bed fusion technique are titanium alloys, ferrous alloys, tantalum alloys, cobalt chrome, and magnesium alloys [6]. Ti-6Al-4V and 316L SS are the most promising candidates for biomedical applications like scaffolds and orthopaedic implants.

Table 1 represents the physical and mechanical characteristics of additively manufactured metals currently utilised in implant applications particularly orthopaedics [7]. Obviously, the metals have high mechanical properties than true bone due to higher relative density. These mismatches induce a "stress shielding" effect in which the scaffolds protect the regenerating bone from mechanical stress, causing adjacent bone necrosis and implant loosening [8].

1.2. Tissue Engineering of Biomaterial Scaffold. Tissue engineering is a technique that involves using donor healthy tissue and biomaterial scaffold techniques to produce bioartificial tissues in vitro and changing cell development and function in vivo [9–11]. To support effective binding, motility, and production of intrinsic extracellular matrix (ECM) components by cells, biomaterials for biomedical applications must have controlled surface shape, porosity, and biocompatibility. Scaffolds, signals, and cells are the basic components of the tissue engineering paradigm [12–15]. These three parts may be used together or separately to create tissues in an infinite number of configurations. However, as the intricacy of a design grows, translation becomes more difficult [16–18]. An acellular scaffold, for example, needs far less time and money to obtain regulatory approval than a drug-eluting scaffold that has been preseeded with stem cells. These three key aspects of orthopaedic tissue engineering are discussed in this section.

2. Materials and Methods

2.1. Nanobiomaterial. According to study, molecular behavior at nanoscale levels limits all living systems. The size, folding, and patterning of nanoscale materials such as lipids, nucleic acids, proteins, and carbohydrates determine their characteristics [19–22]. The scaffold of the extracellular matrix (ECM) is shown to be substantially influenced by cell organisation and other tissue properties. The ECM has a hierarchical structure that spans numerous orders of magnitude in terms of geographical and historical organisation (nm to cm scale) [23–26]. Our bodies' cells are more likely

Table 1: Physical and mechanical properties of metal alloys.

	Ti-6Al-4V	Stainless steel	CoCrMo alloy
Density (g/cm^3)	4.42	8	8.3
Ultimate tensile strength	860	485	655
Yield strength	795	172	450
Elastic modulus	100	193	220
Elongation	10	40	8

to interact with nanostructured surfaces as a result of these variables. As a result, nanoscale structural components are being investigated as biomaterial candidates. In the literature, smaller grain sizes of the ceramic have been linked to higher bone cell activity. When compared to standard (grain size in micron) ceramic formulations, ceramics made independently from spherical nanometer particles of titania, alumina, and hydroxyapatite enhanced in vitro osteoblast adhesion [27–29]. Smaller ceramic spherical grain sizes (and hence surface spherical bumps) have also been proven to stimulate osteoblast activity. As a consequence, the ability of nanophase ceramics to increase bone cell activity was shown to be restricted to below 100 nm [30–33].

In vitro, osteoblasts (bone-forming cells) deposited more calcium on nanophase ceramics than osteoclasts (bone-resorbing cells), but osteoclasts (bone-resorbing cells) performed better. On nanophase alumina and titania, osteoblasts deposited more calcium than on standard ceramic formulations [34–37]. Nanophase ceramics boosted tartrate-resistant acid phosphatase production and the creation of bifurcation pits in osteoclasts when compared to regular ceramics. The particle aspect ratio is another design consideration for orthopaedic nanoparticles. When consolidated substrates made from nanofibrous alumina (length > 48 nm and diameter: 3 nm) were compared to similar alumina substrates made from nanospherical particles, in vitro osteoblast activities were significantly increased. This finding implies that the fibrous aspect ratio, as well as the bone grain size, is critical for nanophase ceramic replication [38–41].

Tissue engineering is gaining popularity as a feasible replacement for standard bone repair techniques. Nanobiomaterial-based bone tissue engineering is still in its early stages, but it is progressing quickly [42–44]. Recent advances in the capacity to convert current ordinary materials to nanoscale properties and accelerate the production of new bone have opened up exciting new prospects in bone tissue engineering [45–47]. Nanophase materials might be employed to improve scaffold mechanical characteristics to match those of genuine tissue, as well as promote bioactivity and tissue integration.

2.2. Bioceramic-Based Composite Scaffolds. Bioactive composite like hydroxyapatite (HA) and tricalcium phosphate (TCP) are the material which has low brittle and with poor mechanical characteristics even in their nonporous condition. These materials are made increasingly weaker by the holes in them. Sintered HA loses a lot of strength when it has a lot of porosity (.50 percent). A beneficial strategy is to reinforce and solidify HA with a little quantity of biocompatible glass, which can considerably improve sintered object strength and hardness. They can be termed composite cellular carriers since the glass strengthens the bioactive bioceramic cell carriers; despite its modest quantity, they function as the secondary phase [48, 49]. Bioactive glass enhances a scaffold's mechanical qualities while preserving the osteoconductive porous ceramic structure. Bioceramic materials have advanced dramatically during the last few decades. Because no material with mechanical, degradation kinetics, or bioactive characteristics equivalent to genuine tissues has yet to be discovered, bioceramic is a hot topic of research. In addition to chemical and crystallographic features, this covers a wide range of geometric, topological, and bioactive attributes [50]. The present state of knowledge regarding bioactive ceramics like HA, TCP, and bioactive glass permits the practical use of their optimum geometrical compositions in the field of dentistry and orthopaedics.

2.3. Bioceramics and Biopolymer Nanocomposites. Natural biopolymers are gaining popularity in tissue engineering due to their biological recognition, which may help cells adhere and operate better [51–53]. They have weak mechanical qualities, though. Because mechanical characteristics of a scaffold are critical for bone tissue regeneration, natural polymer scaffolds must be enhanced in mechanical strength and biological properties [54]. Hydroxyapatite (HA), tricalcium phosphate (TCP), and calcium phosphate are among the bioceramics that are increasingly getting incorporated into endogenous materials to increase mechanical behavior. Because they closely match the essential constitution of bone, collagen and calcium phosphate composites have sparked a lot of attention. Cunniffe et al. created a novel collagen–nHA nanocomposite scaffold using suspension and immersion techniques. The suspending approach was used to create composite scaffolds that seem to be up to 16-20 times tougher than fibre (5.50 ± 1.70 vs. 0.30 ± 0.09 kPa). According to the in vitro results, there was no great disparity in cell number between the suspension technique nanocomposites and the collagen control nanocomposites [55–57]. In case of mechanical characteristics and biological activity, the collagen–nHA nanocomposite scaffold surpasses the collagen control scaffold, suggesting that it might be used as an allografts alternative in orthopaedic stem cell therapy. To increase the mechanical feasibility of this unique bioceramic, researchers from all around the world are undertaking rigorous experiments [58]. Future biomimetic applications may require composite biomaterials, such as ceramics and polymers in various combinations. PLA and HAp synergistically composites have a lot of promise in load-bearing applications.

3. Methods

3.1. Additive Manufacturing (3D Printing). Sachs et al. in 1989 at the Massachusetts Institute of Technology (MIT) have pioneered the additive manufacturing (3DP) technology for creating metallic, ceramic, and plastic products. In additive manufacturing, an extruder ejects a binder solution (organic or water-based) over a specified region on the platform, and a roller transfers a predetermined thickness of ceramic powder on a build platform. Before sintering, the binder develops a permanent link between the particles and the solution by stimulating a reaction between them [59]. The extruder is guided by the machine instruction language derived from the stereolithography file known as "standard triangle language" which has an acronym of STL. When the first coat is complete, the build surface is lowered, a current coating that the layer is deposited over the last layer, and the printing head pours the cement in a precise route [60]. This technique will be followed till the whole section is finished. The printer eliminates the scattered particles from within and around the green superstructure once the printing process is completed to reveal the printed object.

The concentration, quantity of the binding material drop, and viscosity of the printed scaffold are all influenced by the density of the platform or powder bed after the powder has been distributed, particle size, surface finish, and morphology, and the surface tension of the powder and the binder in 3DP [61]. The parameters given above must be substantially changed when using 3DP to create a structure out of a unique bioceramic composition. The binder, which can be made of water or organic ingredients, physically bonds the particles or initiates the molecular setting process [62, 63]. Excessive binder breakdown generates a lot of gas, which can split and damage printed materials, particularly in thin areas of the substructure. Sintering is a posttreatment procedure that removes the natural binder while maintaining the mechanical properties of the printed product. Depending on the binder percentage, sintering causes volumetric shrinkage. For a smooth particle flow across the platform, a well-packed filler material, and fine details in the created scaffold, powder thickness and volume fraction are necessary. Smaller scaffold particles provide finer mesoscopic features, more precise printing, and finer surface treatments, but due to van der Waals forces, they tend to aggregate, resulting in poor ductility and binder integration.

Larger particles spread more readily in the powder bed, enabling higher binder penetration. On the other hand, excessively sizable particles that flow easily result in low spread powder stability and density in the platform. During the printing process, the flowability of powder is improved by particle roundness. Appropriate recoating (spreading the powder by printing layer by layer) may be performed with acceptable permeability, resulting in a light coating and greater printing accuracy. A press-rolling process of the powder has been used to promote flow properties; however, in the latter instance, the liquid content from the solution must be vapourised before the binder is inserted. The amount of binder extruded from the extruder, the size of the drops, and the quantity of adhesive soaked by the powders define the voxel size or printing resolution. The printing resolution is also affected by the wettability of the powder and binder. Excessive binder spreading (poor resolution) occurs from high wettability, whereas low wettability results in insufficient particle integration and as a result, a feeble green body. The degree of wettability is affected by the kind of binder and organic adhesive molecular weight, as well as particle surface chemistry and energy.

In the 3DP approach, two types of binders are usually used: acid-based binders and organic-based binders. The PLA (poly lactic acid) is an organic-based binder. For calcium phosphate powders, acid-based binders have been widely utilised to induce a hydraulic setting. Although sintering is not necessary in this procedure, the resulting objects are highly brittle and must be postprocessed to become mechanically stable.

Scalability to huge sizes up to several metres is one of the benefits of three-dimensional printing in the manufacturing of bioceramic scaffolds. Other benefits of 3DP include its ease of use, low cost, and control over pore geometry and pore size, and because the print is supported by loose particles all around it, there is no need for a framework or additional base to link the scaffolds. A key demerit of 3DP technology is the extensive optimization required to fabricate a robust scaffold with specified porosity design. Furthermore, selecting an appropriate binder is problematic, as is removing the binder stuck inside the tiny pores. Final scaffolds have limited resolution, rough surface quality, low density, and impaired mechanical strength as compared to slurry-based methods, such as stereolithography. For a very porous scaffold printed using the 3DP process, the smallest pore size attainable is roughly 300 μm. 3DP is not a good technology for processing advanced ceramic materials because of its poor resolution. Another difficulty with the 3DP approach is removing loose particles from tiny holes (580 μm), which might be easily damaged. In other cases, the loose particles are sintered inside the pores, generating pore blockages and reducing the scaffold's total porosity, potentially impacting tissue development.

3.2. Fused Filament Fabrication of Scaffold. Fused filament fabrication (FFF) is the most optimistic, precise, and trustworthy scaffolding method to develop a complicated structure. Presently, FFF is a widely used 3-dimensional printer. Printing materials frequently employ polymer-based building components [64]. In a variety of 3D printing applications, metals, composite materials, and even ceramics are employed. Solidworks 2016 (DassaultSystèmes, France) was used to generate the orientation scaffolds. Scaffolds were then constructed using a FFF machine and PLA filament purchased from a local store. An extruder's hot nozzle with a diameter of 0.4 mm was equipped to melt the filament. The molten material was ejected onto a metallic substrate by pushing the extruder in a programmed pattern to create the required form and shape.

After finishing a layer on the same platform, the extruder returns back into its last position and began to create the next layer. All printing variables, including layer thickness, printer head velocity, PLA filament feeding rate, and distance between neighbouring filaments, were established and preset prior to printing. The direction of filament deposition toward "axial" (x) is linked to printing; the orientation perpendicular to the axial in the surface of the printing layers is known as “transverse” (y). Finally, the out of plane is referred to by the z-direction. The mechanical reaction of uniaxial 3D printing is demonstrated in this article. The printing element deposition is consistent at all levels.

3.3. Scaffold Alteration with HAp after Fabrication. The PLA scaffolds were then modified with HA nanoparticles that had previously been generated. To achieve homogeneous dispersion of HA nanoparticles over the PLA scaffold surface, a simple method of moderate heating followed by sonication was adopted. We put forth a lot of effort to make the depositions consistent. We modified the settings for modifying the PLA scaffold surface with homogenised nano-HA after multiple trials and mistakes. To create homogenised nano-HAp, the synthesised HA was first ball milled for 6 hours (at 300 rpm) in a planetary milling machine under dry conditions using 2 mm zirconia balls (Retsch PM100, Germany). Following that, 50 mL deionized water and 1 g finely dispersed homogenised HA nanoparticles were combined. After 10 minutes in the HA sterile water mixture, the scaffolds were stirred continuously at 70 degrees Celsius. The scaffolds were sonicated, then dried, and heated at 72 degrees Celsius for 15 minutes. After chilling for 15 minutes at room temperature, the modified PLA-HA scaffolds were sonicated in DI water for 15 minutes (at room temperature). In huge amounts, unattached HA nanoparticles were washed away. After that, the scaffolds were dried and used for more study. A single flat-surfaced PLA scaffold filament was revealed during SEM inspection. Due to HA inclusion, the smooth PLA surface becomes rough following treatment with nano-HA. A number of trial and error experiments were used to perfect the integration of HAp nanoparticles into the PLA scaffold surface. Excessive HA nanoparticle incorporation may result in scaffold pore blockage, which is undesirable for biological purposes.

4. Applications of Nanocomposite Biomaterial

Nanocomposite biomaterials were widely used in the field of orthopaedics; natural polymers are being used in the field of bone tissue engineering. Chitosan, alginate, starch, and gelatin are some of the popular natural polymers, and synthetic polymers like poly lactic acid (PLA), poly propylene fumarate (PPF), and polycaprolactone (PCL) are also used for bone tissue engineering. Nanocomposite hydrogel based on the biocompatible electrospinning which has high potential for mimicking the nanoarchitecture of bones was exclusively implementing methodology for fabrication of more than 8000 medical devices and 40000 pharmaceutical preparations. And therefore, some of the research proves that the electrospun hydrogel composites for an osteoconductive scaffolding achieve the better characteristic parameters. Nanohydroxyapatite is the most popular bioceramic material used for bone graft substitute because of its biocompatibility and osteoconductive properties. Zirconia-alumina is another familiar composite which has been widely used for orthopaedic implants particularly the ceramic hip prostheses used in hip arthroplasty.

5. Conclusion and Future Scope

With the quick advancement of nanotechnology in the past decades, the investigation of nanocomposites has progressively become significant in the advancement of new materials for cutting edge applications. To satisfy the developing requirements of multifunctional materials, nanocomposites are the best decision as these are not just the adaptable class of materials, yet in addition have an elevated degree of incorporated affiliation. It is a multidisciplinary field which incorporates the information on logical foundation as well as technological viewpoints to make clearly designed materials through nanolevel structures. These materials are reasonable materials to satisfy the arising needs emerging from logical and technological progresses. Exceptional possibilities of nanocomposites can be exemplified by the huge speculations from throughout the world. Therefore, nanocomposites are supposed to create vast changes in the world economy and business. The significant angle is that it gives a conceivable advantage to a large number of medical field and its associations. Apart from the medical field, the advancement of nanocomposite fabrication through the additive manufacturing has also been converged in the area of modern manufacturing like automobile, aeroplanes, structural components for windmill blades, lightweight sensors, and batteries.

Data Availability

The data used to support the findings of this study are included in the article.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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