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A Review on Chemical Synthesis and Density Enhancement in HAp / TiO2 Implants

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Abstract: ***Owing to the excellent mechanical properties , good strength , low density and low toxicity in body fluid, most implants used are based on titanium and its alloys. They don't really, though, have high conductivity and osteo-integration. When using biocompatible and bioactive coatings, the compatibility and bioactivity of the implant material can be boosted. HAp, which is commonly evaluated for its chemical inertness and osteoinduction, is among the most used coating materials that meet the above requirements. For good clinical results, significant scientific findings, and a clear regulatory pathway, research and development of porous structures continues. Although not all applications suit a single size distribution or patterned structure, the majority of porous and textured biomaterials used in medical devices share the common feature of interlinking spaces that facilitate the transfer of nutrients and facilitate the differentiation and proliferation of cells.Safe graft interaction with the surrounding host cell decreases micromotion-induced inflammation and supports steady growth of fibrous content that facilitates healing and reduces disease. So far, many porogenous materials such as napthelene and camphor have been used to establish porosity. When exposed to high temperature, these porogenes will escape from the material that causes Inter communication pores in the material.***

Hydroxyapatite (HAp) belongs to a biologically active moving charges which provides a solid link with the tissues of the surrounding body. One of this material 's drawbacks is that it has lower strength. Titanium oxide (TiO2) is a metal that belongs to the reinforcing agents material class and does not respond to the tissue surrounding it.TiO2's tensile characteristics is usually high and, as an implant unit, can be a good replacement. Efforts have been made to make a combination with better surface quality of both HAp / TiO2 biomaterial device and porosity HAp is commonly used as an implant for the reconstruction of bones, as a covering for metal substrates and as a drug-controlled release.

Keywords: Hydroxyapatite, Biocompatibility, Bioactive, Bioinert, Porosity

I. INTRODUCTION

A biomaterial is any product supposed to intervene with organic procedures for a scientific reason-either a healing one (treatment, augmentation, reconstruction or alternative of a body's tissue feature) or a diagnostic one. Today, it plays an important role in medicine — restoring function and promoting recovery for individuals following injury or illness. Biomaterials may be natural or synthetic, and are used to help, improve or replace damaged tissue or biological function in medical applications. Over the direction of its records it has passed through constant and robust growth, with many groups investing widespread sums of money in developing new merchandise. The technology of biomaterials contains additives of the disciplines of drugs, genetics, chemistry, tissue engineering, and substances. It has skilled regular and steady boom during the direction of its lifestyles, with numerous organizations making an investment large quantities of cash in growing new goods. Biomaterials studies combines elements of the biology, genetics, chemistry, tissue engineering, and substances disciplines.

By nature, biomaterial is 'a non-drug substance appropriate for use in systems that increase or replace body tissue or organ function.' For extended periods of time, these products are capable of being in contact with body fluids and tissues, while causing little to no adverse reactions. Metals, ceramics, plastics, glass, and even living cells and tissue can all be used to form a biomaterial. To use in pharmaceutical products and devices, they may be reengineered into molded or machined parts, coatings, fibres, films, foams, and fabrics. These are also biodegradable, and others are bio-absorbable, meaning these are slowly removed from the body after a function has been fulfilled.

A. Biomaterials Classifications

When a synthetic substance is implanted inside the human body, tissue responds to the implant in different ways, depending on the type of material. The tissue contact function, depends on the tissue response to the surface of the implant. They are bioinert, bioorganic, and bioactive.

1) *Bioinert Biomaterials:* The term bioinert refers to any substance that has limited contact with the surrounding tissue once inserted in the human body, examples of which are stainless steel, titanium, alumina, partially stabilized zirconia and ultra-high molecular weight polyethylene. Generally speaking, a fibrous capsule may shape around bioinert implants, so its biofunctionality depends on tissue integration through the implant
2) *Bioactive Biomaterials:* Bioactive refers to a material which interacts with the surrounding bone and, in some cases, even soft tissue when placed within the human body. This occurs over a period of time-based surface kinetic change, caused by their implantation within the living bone. The ion – the exchange of reaction between the bioactive implant and the surrounding body fluids – results in the creation of an implant layer of biologically active carbonate apatite (CHAp). Such products are mainly used in synthetic hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$].
3) *Bioresorbable Biomaterials:* Bioresorbable refers to a substance that tends to dissolve (resorbed) and is gradually replaced by advancing tissue (such as bone) upon placement inside the human body. The tricalcium phosphate [$Ca_3(PO_4)_2$] and polylactic – polyglycolic acid copolymers are common examples of bioresorbable materials. Other popular materials used over the last three decades include calcium oxide, calcium carbonate and gypsum. Polymers such as polyurethane (PUR), poly (lactic co-glycolic acid) (PLGA), polylactide (PLLA), poly-DL-lactide (PDLLA) are also desirable materials for implant applications, as they provide cell adhesion, attachment, proliferation and differentiation conditions that are favorable. Biodegradable polymers are also advantageous for scaffolds because of their flexibility to control the rate of degradation through copolymerisation. However, their bioactivity and mechanical strength are disadvantages for applications involving load bearing. Metal and its alloys, such as titanium, stainless steel, tantalum, and magnesium, demonstrated a high tensile strength that is ideal for bone replacement load. In the case of dense titanium, the possibility of implant loosening is a major obstacle due to the significant difference between the tensile strength of titanium and the natural bone. One way to lower the tensile strength is to create a porous metallic structure by changing its porosity. Studies on the manufacture of porous metallic have resulted in several changes to decrease the tensile strength and at the same time give adequate mechanical strength for bone replacement. Porous structures on metallic materials for long-term clinical success can have many advantages. Second, the porous structure helps bone to expand into the pores and the artificial implant to be locked for better fixing. The interconnected structure facilitates cell adhesion and keeps cell growth going. Ceramics have been studied for bone graft scaffolds, such as calcium phosphate and bioactive glass, which have shown promising bioactive properties. Calcium phosphate ceramics, for example, demonstrate excellent bioactivity, being osseo-conductive and biocompatible. Nonetheless, some disadvantages for bone implant applications are low strength, brittleness, in-elasticity, low impact resistance and low toughness. The area of Biomaterials moves to biologically "active structures," to enhance their efficiency and extend their use. Biomaterials as a scaffold had been combined with autologous cells (i.e. tissue engineering) to make tissue replacements extra "alive" and more reactive to biological environment. greater currently, large hobby has been shown within the advent of "clever materials' which might be able to educating the movements of adhered or encapsulated cells with the aid of releasing bioactive molecules into the local environment or by way of extracellular protein/peptide mimetics incorporated into the deliver substrates. A spread of architectural functions which include permeability, pore size and porosity play a main function in this boom. Porosity is characterised as the proportion of void space in a solid and is an independent morphological belongings of the material. developing porous material may have three forms of pores: pores which might be closed, pores through and pores blind. The closed pores don't appear to be fluid to be had. within the cloth the blind pores terminate. The pores thru are those which make the most passage of fluids possible. The obvious porosity covers most effective pores via and blind. Porosity that includes closed pores has extensive impudence on a fabric's mechanical residences, open porosity has its direct effect at the likelihood of perfect and unwanted fluids, cells or bacteria being penetrated. due to their possible capacity to sell tissue ingrowth, porous metals with an interconnected pore structure are of particular interest for orthopedic implant programs. Pores are required for tissue formation, as they allow cell migration and proliferation, as well as vascularization. similarly, a porous floor increases mechanical interlocking at this essential interface between the implant biomaterial and the underlying herbal tissue, offering more mechanical stability. consequently, approaches in scaffold design often try and assemble hierarchical porous systems to acquire desired mechanical function and mass transportation (i.e., permeability and diffusion) homes, and to generate those structures within arbitrary and complex anatomical three-dimensional (three-D) shapes. Mass-transport standards for cell vitamins, porous cellular migration channels and mobile attachment surface capabilities include a porous fabric shape. Porosity is a major concern in the manufacture of porous scaffolds as it affects the mechanical properties of the implant (e.g. tensile strength) as well as the biological efficiency of the implant. Porosity will strengthen the interlocking mechanism for the new implant's stability and immobility.

In the framework of a risk assessment process, medical devices and the materials they are made must be analysis in order to prove their nature of biocompaibilirty. Toxicity-related health concerns can be measured using the ISO 10993 set of international standards for biological evaluation of medical devices. In addition to general in vitro cytotoxicity tests, it also addresses more detailed in vitro genotoxicity tests, blood contact, and irritation. In addition, in vivo pain and sensitization tests, haemocompatibility, genotoxicity, implantation, and systemic toxicity can be performed in order to measure their nature of toxicity.

II. REVIEW OF LITERATURE

Bone is a strong and calcareous connective tissue that shapes the body's skeleton, which has the power to constantly preserve an individual's life. Intake of unhealthy diets and lack of physical activity have significant bone-related complications, such as bone diseases, fracture, aging and trauma[1,2]. A number of researchers created bone replacements from bioactive and biocompatible materials that have similar physiochemical and biomechanical properties to natural bone. Such replacements solved problems such as immunological reaction, donor supply and transmission of diseases[3-5]. A human skeleton consists of the phase organic (proteins) and the phase inorganic (minerals). The organic phase is generally a biopolymer comprising glycoprotein, proteoglycans, glycosaminoglycans, and type-I collagen, and the inorganic phase consists mainly of hydroxyapatite (HAp) Ca_{10} $(PO_4)_6(OH)$. HAp is the predominant inorganic stage of the bone (55-65 per cent), and has drawn researchers' interest over the years due to its biochemical resemblance to natural bone and its ability to treat bone deficiencies[6,7]. Numerous HAp-based polymer composite scaffolds have been produced in the last decade. Because of their biocompatibility, the polysaccharide-based HAp composites had gained a lot of interest[8-10]. Recent studies have also shown that ceramic bioactive nanocomposites based on polymer have established strong biocompatible and osteogenic properties and have shown improved mechanical strength. Polymeric bioactive nanocomposites were also used for a large part in biomedical applications[11,12]. HAp ($Ca_{10}(PO_4)_6(OH)_2$) has lately been used for a huge range of biomedical packages such as drug launch control matrices and bone tissue engineering materials [13,14]. HAp is the main inorganic component in natural bones and can be synthesized by chemical precipitation, reaction of the solid state, hydrothermal synthesis, sol – gel route and other routes[15]. Hydroxyapatite (HA) is a bioactive replacement bone used for biomedical applications. One approach to use HA for application of bone implants is to coat it on titanium (Ti) implant. Due to the normal TiO_2 formation on the Ti-based surface, wear and corrosion resistances of Ti-based materials are higher than those of any other material. Though TiO_2 is bioinert in physiological conditions, Ti-based implants often fail after servicing for 10–20 years. Error modes include bone fracture around implanted materials (because of lower bone elastic modulus than that of the implant), implant wear or degradation, inflammation and infection[16]. In addition, naturally formed TiO_2 has low osteoconduction[17,18], which causes loosening of implants leading to failure[19]. One solution is to use Ti with a coating of nanostructured hydroxyapatite (HA) to provide high bioactivity and improve bone ingrowth. Various hydroxyapatite (HA) coating methods have been investigated on the Ti surface, such as Ti soaking in simulated body fluid (SBF) (natural imitation of HA forming), plasma spraying, sol-gel deposition in HA particle solution, pulsed laser deposition, high isostatic pressure and electrochemical deposition[20-27].Porous materials with controlled stiffness can be used to improve the mechanical stability of bone tissue implants. This porosity can help with implant fixation, in addition to increasing durability, by allowing bone growth[28]. However, the design and manufacture of these porous materials may be a major challenge as both mechanical and biological requirements must be taken into consideration. Several processing methods have been used to produce metallic materials with controlled porosity[29-31], such as powder sintering and pressure pore expansion. However, these methods were often used to manufacture materials with a random distribution of the pore. Porosity is characterized as the proportion of void area in a strong[32] and is an impartial morphological assets of the fabric. Pores are vital for the formation of bone tissue, as they enable migration and proliferation of osteoblasts and malignant cells as well as vascularization[33]. similarly, a porous floor will increase the mechanical interlocking among the implant biomaterial and the natural bone surrounding it, providing greater mechanical balance at this vital interface[34].At the moment, one of the most common approaches to lattice structure design includes the use of computer-aided software (CAD)[35,36]. A solid unit cell structure is usually built or extracted from a unit cell library, and copied to produce the lattice structure.

In the framework of a risk assessment process, medical devices and the materials they are made of must be tested for their health. Health toxicity related problems can be determined using the ISO 10993 set of international standards for biological evaluation of medical devices.The assessment can be carried out using different test methods, both in vitro and in vivo. In addition to general in vitro cytotoxicity tests, it also addresses more detailed in vitro genotoxicity tests, blood contact, and irritation. In addition, it explains in detail in vivo inflammation and sensitization tests, haemocompatibility, genotoxicity, implantation, and systemic toxicity.

A. In vitro Cytotoxicity Assays (ISO 10993-5:2009)

ISO 10993-5 (ISO 10993- 5:2009) identifies the general in vitro cytotoxicity assays widely used for the evaluation of biomaterials / medical devices. Cytotoxicity can be calculated by assessment of cell morphology, cell damage, cell growth or cell activity measurement. The following controls should be used in each independent cytotoxicity assay in addition to the normal cell growth control of the cultured cells in the correct tissue culture medium only: a positive control, a negative control and a blank control. The positive and negative controls should be based, respectively, on biomaterials / medical devices which are known to induce a cytotoxic or non-cytototoxic response. Blank control is essential for extracts since this is the extraction medium for preparing the test samples. Genotoxicity testing is suggested when an analysis of the material composition indicates the potential existence of compounds that could interfere with genetic material in the final medical device, or where the chemical composition of the medical device is not known. The in vitro research will contain the three essential endpoints of genotoxicity; that is, gene mutations, aberrations of the structural and numerical chromosomes. Assays for genotoxicity detection are defined in ISO 10993-3:2003 which is currently being revised.

III. METHODOLOGY

A. Synthesis of Hap by Chemical Precipitation Method

Chemical precipitation is achieved by preparing a suspension consisting of 75 g of calcium hydroxide, $Ca(OH)_2$, 510 mL of distilled water and a 40 ml ortophosphoric acid solution, H_3PO_4, in 200 ml distilled water. In order to obtain a hydroxyapatite slurry, H_3PO_4, suspension was applied by dropwise, in conditons of vigorous stirring, over the alkaline solution centered on $Ca(OH)_2$, for 3 hours. The pH was held at 9.5 – 10 during the application, using concentrated aqueous ammonia solution, NH4OH, to achieve a stoichiometric hydroxyapatite (Ca / P = 1.67). The reaction mixture was held for ageing for 48 hours after full addition. The precipitate has been isolated from the suspension by vacuum filtration, washed with distilled water and ethanol to remove any impurities. The filtered cake was dried for 24 hours at 130^{o}C, and then ground in a mortar and pestle to a powder. A TiO_2/hydroxyapatite composite (Ti-HAP) may be prepared using a hydrothermal process with hydroxyapatite and titanium sulfate and tested for methyl orange photocatalytic degradation with ultraviolet (UV) light irradiation of 8 W[37].

B. Characterisation Of Composite by Using FTIR, SEM, XRD

Ti-HAP's properties can be characterized by X-ray diffraction, electron microscope scanning, and an study of Fourier's transform infrared spectroscopy (FT-IR)[38]. Structural properties of synthesized HAp and HAp + TiO_2 powders were calculated using X-Ray diffractometer (XRD) tests. The X-ray diffraction peaks of the HAp and TiO_2 reveal the synthesized nanopowder's hexagonal crystal structure. The elemental analyzes were performed on the pure and TiO_2 doped HAp powders using Bruker-Energy Disperative Spectrometer. The study of field emission scanning electron microscopy (FESEM) and energy dispersive spectrometer (EDS) reveals the morphological structure and elemental composition for HAp samples of pristine and TiO_2 doped organisms. The spectroscopy of Fourier Transform Infrared (FTIR) was used to classify the functional group in pristine and Hap and TiO_2 powders.

C. Development Of Porosity Using Porogen

Porous hydroxyapatite and titanium composite would be prepared by the following methods using camphor as porogen. Camphor would be used as a porogen for the development and control of porosity in composite material. The powder material would be sieved in sieve shaker (Mesh size 50µ) and particle in the size of 50µ would be selected. Weighed amount of calcined HAP/TiO_2 powder would be dried and mixed well with camphor.

D. Preparation Of Palette From Composite

The mixed powders of HAP/TiO_2 powder would be consolidated by uniaxial pressing in high carbon steel mould in a hydraulic press with a capacity of 750MPa. The dry powder to be pressed in a cylindrical die (diameter 12.0 mm) to give the powder in the form of pallet for further studies.

E. Sintering Kinetics Studies

Understanding the sintering behavior of HAP/TiO_2 powder is important, because this allows designing ceramics to study microstructure and mechanical properties [40] The green pellets were sintered at 1250^{0}C for 4 hours at a heating rate of 3^{0}C per minute. The sintered pellet was characterized by using FTIR, SEM, XRD analysis.

F. Apparent Porosity And Bulk Density

The apparent porosity and bulk density of the sintered samples would be measured using Archimedes's principle. Firstly dry weight of the sintered sample to be taken in an electronic balance. The samples were then dipped inside kerosene and kept under a vacuum for two hours to ensure that kerosene filled up the open pores completely and had removed all the air present inside the pores of the sintered pellets. Then, soaked (in kerosene) and suspended weights were measured. Then applying formula Bulk density and apparent porosity would be measured.

G. In Vitro Studies of Snthesized HAP/TiO_2 Composite

The in vitro bioactive evaluation of synthesized Hydroxyapatite Titanium powder was performed in SBF media of pH 7.40 at a ratio of 1mg/ml in a water bath at 37^{O}C. HAP/TiO_2 pellet sintered at 1200^{O}C was taken as the starting material for our study. The important factor during the preparation is to observe that the pH of SBF should be around 7.4 and the ionic concentration of SBF should be equal to that of blood plasma. The pallet of composite would be kept for 7 days in SBF and the layer of apatiate formation can be seen with the help of SEM.

Cytotoxicity can be calculated by assessment of cell morphology, cell damage, cell growth or cell activity measurement. The positive and negative controls should be based, respectively, on biomaterials / medical devices which are known to induce a cytotoxic or non-cytototoxic response. Blank control is essential for extracts since this is the extraction medium for preparing the test samples. [41] The MTT assay can be used to determine the cytotoxicity of: medical device extractable materials, toxic materials, toxins.

The in vitro degradability of the porous HAP/TiO_2 would be determined by their weight loss percentage in a Tris-HCL buffer solution. The Tris-HCL buffer solution was prepared by dissolving 0.1MTris- HCl solution in distilled water. The pH of solution was maintained 7.4 at 37^{0} c by adding 1MHCl. Porous HAP with camphor (5-50 wt %) in the form of pellets were soaked in 24 days in polystyrene bottles containing Tris-HCl buffer solution in a water bath shaker. The weight loss behavior of composites would be recorded in order to see biodegradation activity of the composites.

H. CAD/CAM Modelling of Composites

CAD / CAM systems use an optical camera to take a virtual impression by generating a 3D image that is loaded into a software program and contributes to a computer-generated cast optimized for the reconstruction[39]. Integrated CAD / CAM system for the automated manufacture of preformed dry carbon fibre. An automated preform lay-up program that involves automated ply cutting, handling, lay-up, inspection, and tacking. Process and task planning strategies are then proposed to produce the manufacturing data directly from the component's CAD register, needed by the lay-up system to lay-up a part. This allows operation of the lay-up system directly from the CAD info. A vision system for in-process preform stack inspection against CAD specification and enables the incorporation of CAD data into the vision system[42].

IV. CONCLUSION

HAP/TiO_2 implant device is available and are used as implant device, but one of the major drawbacks is lack of porosity in the implant device. Earlier studies showed that failure of the device occurred in view of inducing porosity in material so by sintering kinetics study a proper correlation between the porosity and mechanical behavior can be studied in detail in future.

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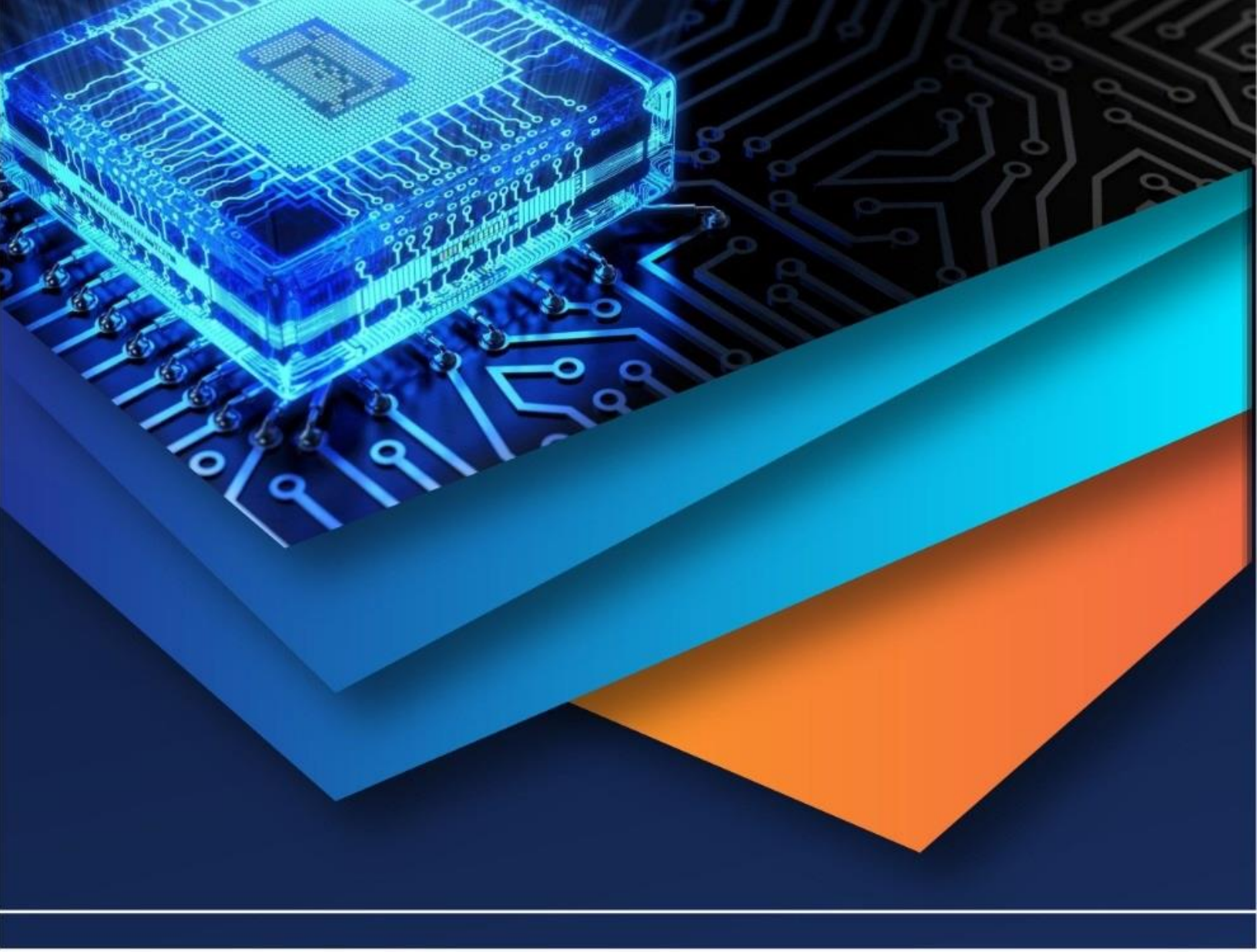

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