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Nanofibers: The Novel Technology

Rohit Balasaheb Jadhav[1], Aasawaree Mane[2], Rupali Rajesh Tasgaonkar[3]
[1]*Yadavrao Tasgaonkar Institute of Pharmacy, Karjat*

Abstract: ***Polymer nanofibers, with diameters in the nanometer range, possess larger surface areas per unit mass and permit easier addition of surface functionalities compared with polymer microfibers. Research on polymer nanofibers, nanofiber mats, and their applications has seen a remarkable growth over the last few years. Unique properties of Nanofibers have attracted for the designing of controlled drug delivery systems due to high surface area to volume ratio, porosity so only we can applied in advance application such as Biodegradable and controlled drug delivery systems. The benefits of the fibrous carriers are site specific delivery of drugs to the body.***
Nanofibers are an exciting new class of material produced using an innovative manufacturing process technology. These fibers are produced from a variety of polymers in geometrical shapes ranging from Nonwoven web, yarn, and bulk structures. The Synthetic polymer Nanofibers are made from Nylon, Acrylic, Polycarbonate, Polysulfones, and Fluro polymers among other polymers.
The biological polymer nanofibers are made from materials such as Polycaprolactum, Chitosan, Polylactic acid, and Copolymer of Polylactic/glycolic acid among other biopolymers. At present, there are three techniques available for the synthesis of Nanofibers: Electro spinning, self-assembly, and phase separation, out of these Electro spinning is the most widely used technique.
The advanced approach for creating Nanofibers made of proteins developed, greatly improve drug delivery methods for the treatment of cancers, heart, and Alzheimer"s diseases, as well as aid in the regeneration of human tissue, bone and cartilage. This review paper reports on fabrication of nanofibers and its characteristics and high tech application in drug delivery, tissue engineering and filter medium
Keywords: Nanofibers, Electro spinning, Fabrication, Polymers, Engineering

I. INTRODUCTION

Fiber is diameter in nanometer range. Nanofibers are a nanomaterial with one dimension less than 100 nm. Wide range of polymers such as polyvinyl alcohol, gelatin, collagen, chitosan and carboxymethylcelulose can be subjected to electro spinning technique to produce nanofibers. Nanofibers have large specific surface area with small pore size and these unique properties showing opportunities in management of wound care applications.
The benefits of the nanofibers are; development of nanofiber layers from different polymer, drugs or growth factors can be incorporated into different nanofiber layers for wound care management. Role of nanofibers in advanced wound care managements are; a) absorption of exudates, b) addition of drugs to the nanofibers and showing anti-adhesive effect. In addition, nanofibers can be used in drug delivery systems to improve control drug delivery of drugs via nanofiber.
The objective of drug delivery systems is to deliver a defined amount of drug efficiently, precisely and for a defined period of time. The new technologies and materials will have a profound impact on drug delivery. Either biodegradable or non-degradable materials can be used to control whether drug release occurs via diffusion alone or diffusion and scaffold degradation. Additionally, due to the flexibility in material selection a number of drugs can be delivered including: antibiotics, anticancer drugs, proteins, and DNA. Using the various electro spinning techniques a number of different drug loading methods can also be utilized: coatings, embedded drug, and encapsulated drug (coaxial and emulsion electrospinning).

A. Properties of Nanofibers

Nanofibers exhibit special properties mainly due to extremely high surface to weight ratio compared to conventional nonwovens. Low density, large surface area to mass, high pore volume, and tight pore size make the nanofiber nonwoven appropriate for a wide range of filtration applications.
A major upsurge in research on nanofibers has taken place most recently due to its high surface area and nanostructure surface morphologies that enable a myriad of advanced applications. Nanofibers have been reported to have marked differences in their thermal and mechanical properties compared to regular fibers and bulk polymers.

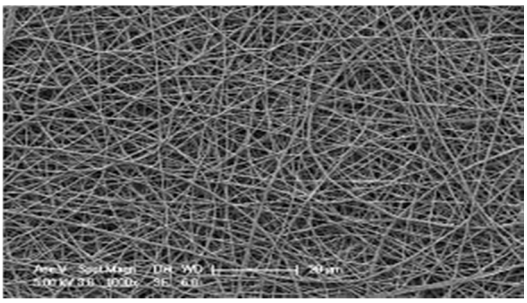

Image No. 1 – SEM of Nanofibers

B. Thermal Properties

There are a few published reports on the thermal properties of nanostructured materials. Thermal analysis has been carried out on a number of electrospun polymeric materials to understand the relationship between nanostructure and thermal properties. DSC studies have indicated that electrospun PLLA fibers have lower crystallinity, glass transition temperature (Tg), and melting temperature (Tm) than semicrystalline PLLA resins. Zong et al. attributed the decrease in the Tg to the large surface to volume ratio of nanofibers with air as the plasticizer. The high evaporation rate followed by rapid solidification at the final stages of electrospinning is expected to be the reason for the low crystallinity. The Tg and the peak crystallization temperature (Tc) of the electrospun polyethylene terephthalate (PET) and poly- ethylene naphthalate (PEN) decreased significantly, while the heat of crystalline melting increased. The decrease in Tg and Tm, and the increase in the heat of melting were attributed to the increase in the segmental mobility. The melting temperature of the PET and PEN electrospun fibers remained almost constant, without any significant variations compared to that of regular fiber forms. PEO Nanofibers have shown a lower melting temperature and heat of fusion than the PEO powder, which is attributed to the poor crystallinity of the electrospun fibers.

C. Mechanical Properties

Electrospun fibers have nano structured surface morphologies with tiny pores that influence mechanical properties like tensile strength, Young‟s modulus, etc. Gibson et al. have found that there is no significant change in the Young‟s modulus of electrospun Pellethane thermoplastic elastomers. When compared with cast films, electrospun elastomers have shown a 40% reduction in the peak tensile strength and 60% reduction in elongation at maximum applied stress. The decrease in the tensile strength has also been reported by Buchko et al. with SLPF fibers. Nanofiber reinforced polymer composites have shown more highly enhanced mechanical properties than the unfilled or carbon/glass fiber filled composites. Young‟s modulus of a nanofiber composite has been found to be 10-fold greater than the pure Styrene-Butadiene rubber. Research on the mechanical properties of nanofibers and their composites from a variety of polymers is essential for a greater understanding on the contributions of nanofibers to the mechanical and performance related characteristics of nanofiber composites.

D. Physical Properties

The simplest comparison between eletrospun Nanofibers, meltblown fibers and spunbonded fibers size. The differences in basic web properties such as fiber area ,basis weights, thicknesses, permeability, and strength. Electrospun Nanofibers have diameters that are 1to 2 orders of magnitude corresponding increase in fiber surface area and decrease in basis weight.

II. TECHNIQUES OF CREATING NANOFIBERS

Three distinct techniques have proven successful in routinely creating nanofibrous tissue structures:
self assembly, phase separation, and electrospinning. The electrospinning method is the most simple and efficient

A. Self-assembly

Self-assembly involves the spontaneous organization of individual components into an ordered and stable structure with preprogrammed non-covalent bonds. Self-assembly, that is, the autonomous organization of molecules into patterns or structures without human intervention, are common throughout nature and technology56. Self-assembly of natural or synthetic macromolecules produces nano scaled supramolecular structures, sometimes nanofibers. Compared with electrospinning, self-assembly can produce much thinner nanofibers only several nanometers in diameter, but requires much more complicated procedures and extremely elaborate techniques. The low productivity of the self-assembly method is another limitation.

B. Phase Separation

Phase separation is a method frequently used to prepare 3-D tissue-engineering scaffolds. Phase separation of a polymer solution can produce a polymer-rich domain and a solvent-rich domain, of which the morphology can be fixed by quenching under low temperature. Removal of the solvent through freeze-drying or extraction can produce porous polymer scaffolds. Phase separation can be induced by changing the temperature or by adding non solvent to the polymer solution, thus called thermal induced or non-solvent-induced phase separation, respectively. Polymer scaffolds obtained by the phase separation method usually have a sponge like porous morphology with microscale spherical pores.

C. Electrospinning Process

The nanofibers can be manufactured by Electro spinning process. Electro spinning is a process that was originally developed in the early 1930s, but did not receive much attention until recent decades.

A typical electro spinning process involves dissolving the drug of interest and a polymer in an appropriate solvent. The solution is then placed in a syringe, and a high voltage is applied. A small amount of the polymer solution is drawn out of the syringe, forming a Taylor cone. Increasing the applied voltage further results in the initiation of a charged fluid jet, which follows a chaotic trajectory of stretching and bending until it reaches the grounded target. A stable jet is formed when the charge is increased above a critical voltage, and there is a balance between the surface tension of the fluid and the repulsive nature of the charge distribution on the surface of the fluid.The process makes use of electrostatic and mechanical force to spin fibers from the tip of a fine orifice or spinneret. The spinneret is maintained at positive or negative charge by a DC power supply. When the electrostatic repelling force overcomes the surface tension force of the polymer solution, the liquid spills out of the spinneret and forms an extremely fine continuous filament. It has the misleading appearance of forming multiple filaments from one spinneret nozzle, but current theory is that the filaments do not split.

These filaments are collected onto a rotating or stationary collector with an electrode beneath of the opposite charge to that of the spinneret where they accumulate and bond together to form nanofiber fabric. The distance between the spinneret nozzle and the collector generally varies from 15 –30 cm. The process can be carried out at room temperature unless heat is required to keep the polymer in liquid state. The final fiber properties depend on polymer type and operating conditions. Fiber fineness can be generally regulated from ten to a thousand nanometers in diameter.

Electrospun nanofibers with a high surface area to volume ratio have received much attention because of their potential applications for biomedical devices, tissue engineering scaffolds, and drug delivery carriers.

Image No. 2 – Electrospinning Unit

D. Polymer-solvents used in Electrospinning

The polymer is usually dissolved in suitable solvent and spun from solution. Nanofibers in the range of 10-to 2000 nm diameter can be achieved by choosing the appropriate polymer solvent system4 . Table 1 gives list of some of polymer solvent systems used in electrospinning.

Polymer	Solvents
Nylon 6 and Nylon 66	Formic Acid
PET	Dimethylformaldehyde
PVA	Trifluroacetic acid
Polystyrene	Water
Nylon-6-co-polyamide	DMF/ Toluene
Polybenzimidazole	Dimethylacetamide
Polyramide	Sulfuric acid
Polyimides	Phenol

Table No. 1

E. Drug Loading

One method to incorporate therapeutic drugs into nanofibers involves solubilizing the drug into the polymer solution to be spun62. Using this method, a loading efficiency of 90% into PDLA nanofibers was reported for the antibiotic drug Mefoxin. Covalent conjugation to polymers represents another method to modulate drug release63. It has also been suggested that the high porosity of nanofibers allows for rapid diffusion of degradation by products64. However, the burst release may also be indicative of the drug being attached only on the surface. As the drug and carrier materials can be mixed together for electrospinning of nanofibers, the likely modes of the drug in the resulting nanostructed products are65:

1) Drug as particles attached to the surface of the carrier which is in the form of nanofibers,
2) Both drug and carrier are nanofiber-form, hence the end product will be the two kinds of nanofibers interlaced together,
3) The blend of drug and carrier materials integrated into one kind of fibers containing both components, and 4. The carrier material is electrospun into a tubular form in which the drug particles are encapsulated

III. MECHANISM OF DRUG DELIVERY

Nanofiber drug delivery systems may provide insight into the direct incorporation of bioactive growth factors into scaffolds. Additionally, drug delivery systems can be combined with implantable tissue engineering scaffolds to prevent infection while repair and regeneration occur. Biodegradable polymers release drug in one of two ways66: erosion and diffusion. Release from biodegradable polymers in vivo is governed by a combination of both mechanisms, which depends on the relative rates of erosion and diffusion. Most biodegradable polymers used for drug delivery are degraded by hydrolysis. Hydrolysis is a reaction between water molecules and bonds in the polymer backbone, typically ester bonds, which repeatedly cuts the polymer chain until it is returned to monomers. Other biodegradable polymers are enzymatically degradable, which is also a type of chain scission. As water molecules break chemical bonds along the polymer chain, the physical integrity of the polymer degrades and allows drug to be released.

IV. APPLICATIONS OF NANOFIBERS

Filtration Nanofibers have significant applications in the area of filtration since their surface area is substantially greater and have smaller micropores than melt blown (MB) webs. High porous structure with high surface area makes them ideally suited for many filtration applications. Nanofibers are ideally suited for filtering submicron particles from air or water. Electrospun fibers have diameters three or more times smaller than that of MB fibers. This leads to a corresponding increase in surface area and decrease in basis weight. Table 2 shows the fiber surface area per mass of nanofiber material compared to MB and SB fibers

FIBER TYPE	FIBER SIZE IN MICROMETER	FIBER SURFACE AREA PER MASS OF FIBER MATERIAL m2/g
Nanofibers	0.05	80
Spunbond Fiber	20	0.2
Melt blown Fiber	2.0	2

Table 2: Fiber surface area per mass of fiber material for different fiber size

E-Spin Technologies, Inc has produced a prototype of activated carbon nanofiber web. PANbased nanofibers were electrospun. Then these webs were stabilized, carbonized, and activated. These activated PAN nanofibers gave excellent results for both aerosol and chemical filtration.

A. *Medical Application*

Nanofibers are also used in medical applications, which include, drug and gene delivery, artificial blood vessels, artificial organs, and medical facemasks. For example, carbon fiber hollow nanotubes, smaller than blood cells, have potential to carry drugs in to blood cells. Nanofibers and webs are capable of delivering medicines directly to internal tissues. Anti-adhesion materials made of cellulose are already available from companies such as Johnson & Johnson and Genzyme Corporation 16 . Researchers have spun a fiber from a compound naturally present in blood. This nanofiber can be used as varieties of medical applications such as bandages or sutures that ultimately dissolve in to body. This nanofiber minimizes infection rate, blood lose and is also absorbed by the body.

B. *Topical Drug Delivery*

Nanofibers for drug and gene delivery application have been used for tissue engineering to improve therapeutic efficacy. in addition, the fibrous surface structure shows strong adhesiveness to mucous layers because their nano-porous structures instantly absorb moisture at mucous layers through nano-void volumes. The superior adhesiveness to word biological surfaces allows Nanofibers to be an ideal candidate for topical drug delivery devices.

1. Vitamins - Electrospun Nanofibers can be used as carriers for delivery of some vitamins to the skin. Usually, vitamins are applied to the skin in the form of topical creams, lotions, or ointments. Here vitamin – E and vitamin-A, were selected as the model vitamins, due to their benefits in cosmetics. Vitamin –A is naturally occurring, and lipid soluble substances, known to be used for the treatment of leukemia, acne, and other skin disorders. Vitamin-E is also lipid soluble vitamin, it shows potent antioxidant ability, owing to the presences of a hydroxyl group on its chromanol ring which can readily donates a proton to reduce free radicals.
2. Protein delivery- Nanofiber to regulate the release of the encapsulated proteins in core. A near Zero order release of platelet derived growth factor-bb (PDGF-bb) can be produced with no associated burst release. In addition, aligned PDGF-bb loaded Nanofibers are fabricated. These aligned drug loaded fibers may simultaneously provide biochemical and topographical cues to the seeded cells, provisions that should prove beneficial for many tissue engineering applications.
3. Nucleic acid- Luu et al. describe the encapsulation of plasmid DNA in a PLA-PEG block co-polymer nanofibrous natrix for tissue engineering purposes81. Approximately 80% of the β-galactocidase receptor gene is released in 20 days. Transfection experiments performed on the osteoblastic cells line MC3T3-E1 demonstrate increased transfection efficiency of the fiber-encapsulated DNA over naked plasmid added to the medium, but lower than that with a commercial transecting reagent. For improving stability of DNA during the electrospinning processes Liang et al. have incorporated solvent-induced compacted DNA in PLA-PEG-PLA triblock co-polymer.

C. *Applications of Nanofibers as Drug Delivery System:*

Desired properties of Nanofibers for application as drug delivery Protect the drugs in the case of systemic application from decomposition, e.g., in the blood circuit.

They should allow controlled release of the drug at a release rate as constant as possible over a longer period of time, adjusted depending on the field of application. Permeate certain membranes or barriers, e.g. BBB. They are supposed to concentrate the drug release only on the targeted body.

Nanofibers have potential medical applications, which include, drug and gene delivery, artificial blood vessels, artificial organs, and medical facemasks. For examples carbon nanofiber, hallow Nanofibers are smaller than blood cells, have potential to carry drugs in to blood cells. Nanofibers are capable of delivering medicines directly to internal tissues. This nanofiber can be used as varies of medical applications such as bandages or sutures that ultimately dissolve in to body. This Nanofiber minimizes infection rate, blood lose and is also adsorbed by the body.

Employing electrospun Nanofibers as drug delivery vehicles has been based on their unique functionally and inherent nanoscale morphological characteristics. A rich variety of therapeutic agents such as antibiotics, anticancer drugs, polysaccharides , proteins,and growth factors have been physically or chemically formulated within the bulk Phase of electrospun Nanofibers or on their surface for accomplishing controlled topical within the defined period of time. Such medicated Nanofibers could be could be applied to various purposes including tissue engineering scaffolds. Recently introduced surface modified designs for drug loading open up the new possibility of constructing more sophisticated drug delivery platforms. **Table 3:** shows Marketed Nanofibers products available.

PRODUCT	DESCRIPTION	MANUFACTURE
Integra	Nano fiberoys bovine type1 collagen/glycosaminoglycons/synthetic polysiolxane based dermal analogue	Intergra Life Science
Nanocell	Nanofibrous microbial cellulose masks	Thaionano cellulose
Apligral	Bovine collagen nanofibrous sponge with neonatal foreskin fibroblasts and keratinocytes	Novartis
Kerlix AMD	Nanofibrous PHMB gauge	Kendall
Dermafuse	Bioactive borate glass nanofibrous dressing	Mo-sci corporation U.S.A
Trans type	Eletrospun nylon Mesh/Collagen/Silicone dermal substitute embedded with allogenic fibroblasts	Advanced Tissue Science
Tegaderm	Eletrosun poly(caprolactone) (PCL)/gelatin/polyurethane/scaffold	3 M Company
Chito Flex	Fabricated chitosan nanofiberous dressing	Hemcon Med Tech.Inc.
Permacol	Dermal matrix of procine nanofibers	Covidien
Allo derm	Condaners a cellular matrix Nanofibers autograft	Life cell corporation

Table No. 3: Marketed Nanofibers products available.

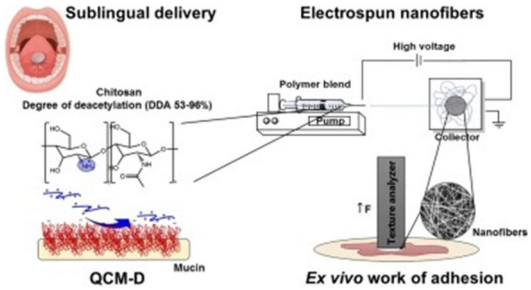

Image No 3 – Sublingual Delivery using Nanofiber

D. Food Packaging

The application of electrospun nanofibers in functional food packaging has become an evolving fascinating area to exploit and develop research for strength and barrier enhancements compared to conventional packaging materials. According to the FDA, food packaging substances derived from electrospun nanofibers materials must possess biocompatibility and nontoxic properties. The developed research is meant for improving antimicrobial activity, rapid sensing and detection on the signaling microbiological and biochemical changes, in order to extend food shelf lives for long-term freshness.

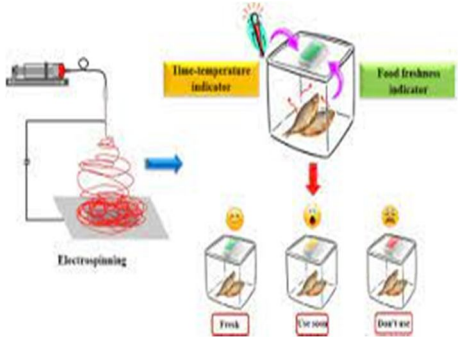

Image No. 4 – Nanofiber in Food Packaging

E. Cosmetics

Electrospinning has the potential for use in various cosmetic applications for example facial masks, perfumes, deodorants and antiperspirants. A common feature of these applications is that they can be used in the form of a membrane which can be easily fabricated by electrospinning. The conceivable of incorporating active ingredients into electrospun nanofibers also makes this spinning process feasible for cosmetic applications. Yet, the application in the cosmetics product from nanofibers textiles material is relatively new. A reported study conducted by Fathi-Azarbayjani et al. (2010) indicated that electrospun fiber materials are influential to replace the conventional materials used in the current cosmetic facial masks. Their work demonstrated an anti-wrinkle nanofiber face mask incorporating collagen, novel vitamin and gold nanoparticles, with a control polymer degradation to discharge the active ingredients once contact with premoistened skin. The study reported that the high surface area to-volume ratio of the nanofiber mask will ensure maximum contact with the skin surface and help to enhance the skin permeation to restore its healthy appearance. The dry nature of face masks increases both the structural stability and their shelf lives when compared to premoistened cotton masks available in the market.

Image No. 5- Nanofiber in Cosmetic

V. CHALLENGES IN NANOFIBERS

The process of making nanofibers is quite expensive compared to conventional fibers due to low production rate and high cost of technology. In addition the vapors emitting from electrospinning solution while forming the web need to be recovered or disposed of in an environmental friendly manner. This involves additional equipment and cost. The fineness of fiber and evaporated vapor also raises much concern over possible health hazard due to inhalation of fibers. Thus the challenges faced can be summarized as10: Expensive, Health hazards, Solvent vapor, Packaging, shipping& handling.

VI. CONCLUSION

Today Nanofibers are at the forefront of nanotechnology. Their unique porous structures and large surface to volume area make them suitable for a wide variety of applications. Nanofiber controlled drug delivery system is becoming the flash news in pharma field. Nano structure delivery architecture are promising candidates that will enable efficient in Targeted and Novel drug delivery. Electrospinning provides the most versatile process to produce nanofibers with a wide range of properties. Potential medical applications include efforts to fabricate electrospun polymer nanofiber scaffolds for nerves, tissues, skin and bone. Still several problems must be resolved for further applications such as the drug loading, the initial burst effect, the residual organic solvent, the stability of active agents, and the combined usage of new biocompatible polymers.

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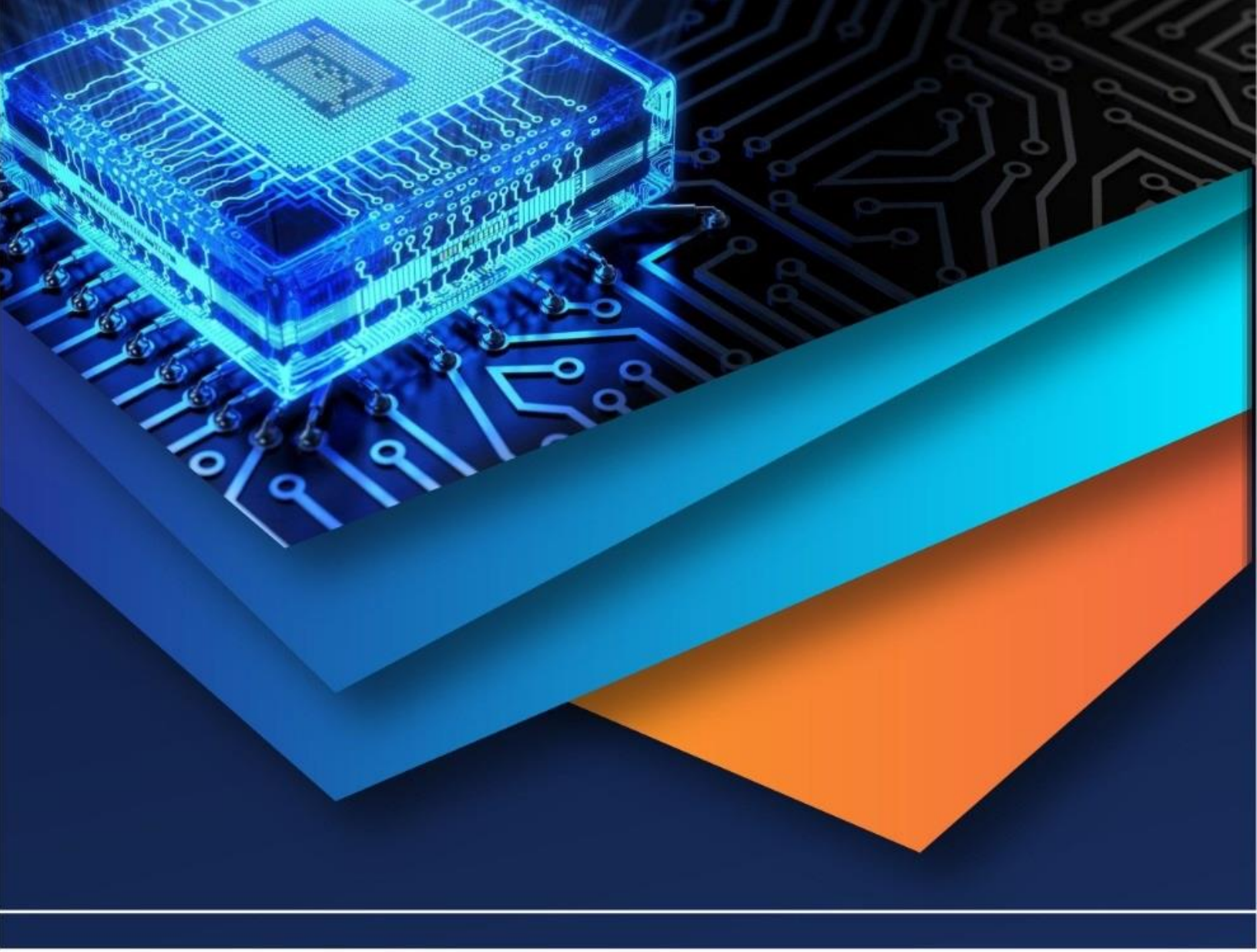

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