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# Novel L-Tyrosine based Polyphosphates with alternating Peptide-Phosphoester Moiety in Bioengineering Action

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***Abstract:*** ***Since by introductory of Lopina et al. in 2005, a biodegradable and biocompatible amino acid such as L-tyrosine based polyphosphates have alternating peptide and phosphoester bonds moieties which are being applicable for potential orthopedic polymeric biomedical and bioengineering materials.***
***In synthetic, L-tyrosine converted their ester then mediated coupling and refluxing at 40℃ under $N_2$ with alkyl or aryl phosphodichloridate to DTH, which on dehydrochlorination polycondensation via proceeds subsequent DTH based polyphosphates.***
***Applying, the physico-chemical characterization (DSC & TGA etc.) studies which reveals that the resultant developed polymers have possess improved chemical/thermal processability, solubility, hydrophilicity and hydrolytic degradation when on drop in local pH value to 6.23-7.4 at physialogical temperature range of 37℃ having concentration of 15mg/ml with at specific time intervals over a period of 7 days.***
***Keywords: Amino acid, L-tyrosine, polyphosphates, degradation.***

## I. INTRODUCTION

In unique chemistry of biological apatite can be synthesized from various calcium orthophosphate such as α- and β- tricalcium phosphate (TCP,$Ca_3(PO_4)_2$) where the hydroxy apatite (HAP,$Ca_{10}(PO_4)_6$ $(OH)_2$ is the main inorganic components of hard tissues such as bone and teeth[1].

Although, study of biological phosphate chemistry is of key importance to understanding many cellulose process such as the hydrolysis of phosphate involved in transcription, cell signalling & respiration[2].

Recently, there has been a high demand of biomaterials in treatment or replacement of damage tissues and organs which leading to many studies on several advanced biocompatible and biodegradable materials, as a protein (gelatin) carbohydrates chitosan based hydrogels loading biphasic calcium phosphate nanoparticles for bone tissue regeneration also have much attention [3-6].

The field of identification of these compounds with biological application can be used as carriers for small molecules or macromolecules like protein (amino acid) moieties *L*-tyrosine based as a novel class of polymeric biomaterials have introduced [7,8], whenever, inhibitors of protein tyrosine phosphates in drugs[9].

The unique chemistry of these polymers is the combination of enzymatically degradable peptide bonds with hydrolytically degradable non-peptide bonds in the polymer backbone. Although, biocompatible have been well reported to exhibit prominent bioengineering and processing difficulties like insolubility in common organic solvent, unpredictable water permeablity and swelling, high thermal transition temperature range.

Introduction of specific non-peptide bonds alternating with peptide bonds in natural amino acid based polymer backbone, which improve chemical and thermal processability, solublity etc.

In engineering the hydrolytic nature of the 'phosphoester' moiety are develop L-tyrosine based polyphosphate with alternating peptide & phosphoesters bonds in polymer backbone[10].

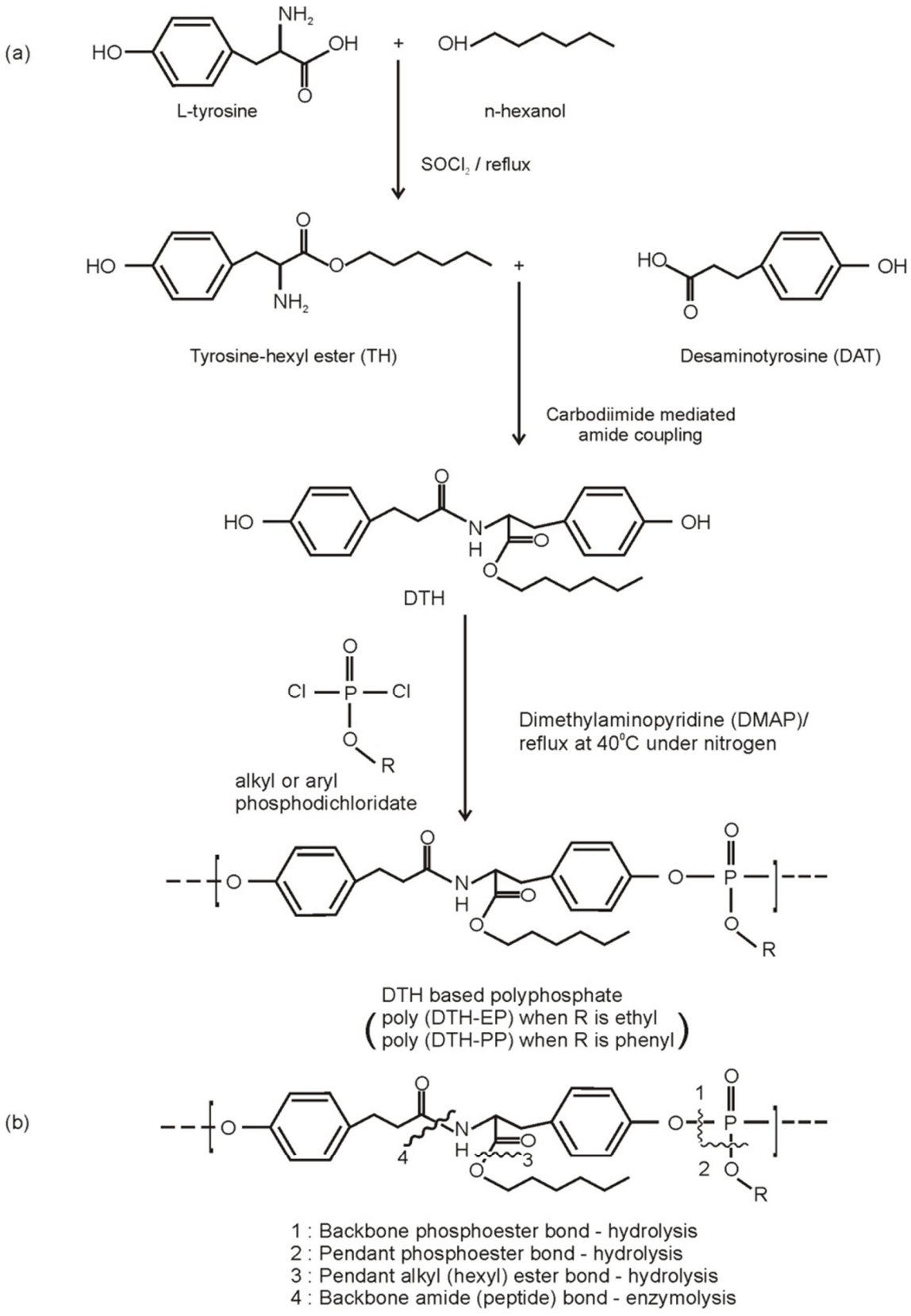


**Fig.1** Chemical structures of L-tyrosine based diphenolic monomer and corresponding polyphosphate polymer, (a) and, chemical nature of polymer digradation, (b).

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In experimental procedures firstly, the amino acid (*L*-tyrosine) is converted into *L*- tyrosine-hexyl ester (TH) and then coupled with desaminotyrosine (DAT), through, mediated solid phase amide to desaminotyrosine –tyrosine-hexylester (DTH), these DTH is further reacted with suitable alkyl/aryl phosphochloridate, like ethyl phosphodichloridate (EP) and phenyl phosphodichloridate (PP) in ratio 1:1, to induced dehydrochlorination-polycondensation reaction in presence of suitable acid acceptor like dimethyle amino pyridine(DMAP), to produce the subsequent DTH - based polyphosphates, naming as poly (DTH-EP) and poly (DTH-PP). Such synthesis procedure are adapted from the work described by Gupta- Lopina[7]. All the solvents are freshly distilled before conducting reactions. The chemical structure of monomer and the corresponding polymer are shown in figure-1. All materials are characterized by molecular weight distribution, DSC &TGA for their glass transition temperature and their thermal degradation properties respectively.

A possible study of hydrophilic nature of the *L*-tyrosine based polyphosphates is obtained by dynamic contact angle measurements by goniometer, for this purpose a clean silica plates are submerged in corresponding polymer solution for 12 hr to ensure uniform coating of the surface with polymer film. These surfaces are then dried under vaccum for about 8-10 hr and subsequently dried under a flow of nitrogen ($N_2$) for 1hr prior to dynamic contact angle analysis. The effect of the *L*-tyrosine based polyphosphate degradation on local pH is considered to be an important factor to be studied for judging potential biomaterial application. Since, the hydrolytic degradation of these polymer is conducted by exposing the polymer to phosphate buffered saline (PBS; pH 7.4) at temperature range 37℃. The drastic changes of local pH as a result of acidic degradation products has been found to have a detrimental effect both on the polymer properties and on the surrounding tissue, regarding several intended biomaterial applications of clinically established biodegradable polymers like polylactate (PLA), polyglycolate (PGA) and polycaprolactone(PCL) etc.

## II. RESULTS AND DISCUSSION

### *A. Solvent Behavior and Polymer*

The *L*-tyrosine polyphosphate having readily solubilities in a variety of common organic solvents such as $CHCl_3$,$CCl_4$,THF and $C_2H_5OH$ and $H_2O$. About, 8-10 gm of polymer could be readily dissolved in 100ml of any of the given organic solvents at room temperature ($25^0$C) to give a transparent yellowish solution with excessing of polymer and soln. is found to become increasingly translucent and viscous. It is possible solvent cast films of the protein based polymer from the corresponding soln., indicating the potential advantage of the polymers which undergo to chemical processing of *L*-tyrosine polyphosphate in use of biomaterial fabrication or fixture. Where the partial solubility of the polymer in water or ethanol suggested amphiphilic behaviour which may be usefull for aquous based drug delivery application.

### *B. Hydrophilic Nature & Hydrolytic Degradation studies of Polymer*

The hydrophilicity and degradability of protein (*L*-tyrosine) based polyphosphates have been verified by dynamic contact (advancing & receding ) angle measurement for water on corresponding polyphosphate surfaces, to suggested considerable wetting of the surface by water (hydrophilic nature), for poly(DTH-EP) & poly(DTH-PP) having the average advancing contact angle about $70^0$ & $78^0$ where the receding with $15^0$ &$19^0$, respectively.

The hydrolytic degradation studies of protein (*L*-tyrosine ) based polyphosphates have established by buffer incubation experiment. In degradation study (as figure-2) the physical molecular mass (Mw; 5,000-15,000) loss of the polymer pellets in ranged pH 7.4, at temp. $37^0$C, is followed to one weak. Where, the vial containing the degraded products which is subjected to freeze drying for 12 hr. for ensuring the complete removal of residual water from vial and hence vial containing residual degraded polymer. The trace amounts of salts components is dissolved by adding of about 10ml of $CHCl_3$. Then the polymer soln. is filtered off and filtrate put back into its corresponding vial and subsequently the solvent was evaporated from the filtrate under vaccum to obtained dry residual polymer as powder. The weight of this dry polymer residue along the vial is determined with comparing the initial weight of the vial plus the initial dry pellet. Thus, from these value, the mass loss of the pellet due to hydrolytic degradation can be calculated. The experimental studies have shown that the polyphosphates loose over 80% of their initial weight over a period of 4 days. The poly (DTH-PP) apparently seemed to have a slightly lower degradation rate than poly (DTH-EP) which may be aspected to the slightly more hydrophobic structure of poly (DTH-PP) compared than poly (DTH-EP) ,due to presence of more aromatic group in form. These fast hydrolytic degradation nature of the *L*-tyrosine based polyphosphates can be attributed to presence of hydrolytically unstable phosphoester groups in the polymer backbone and also as pendant chains. The pure protein *L*-tyrosine showed no such hydro-degradation characteristics and hence the introduction of hydrolytically unstable phosphoester moieties in an protein *L*-tyrosine backbone provided a way to improve degradation characteristics of such protein *L*- tyrosine phosphates.

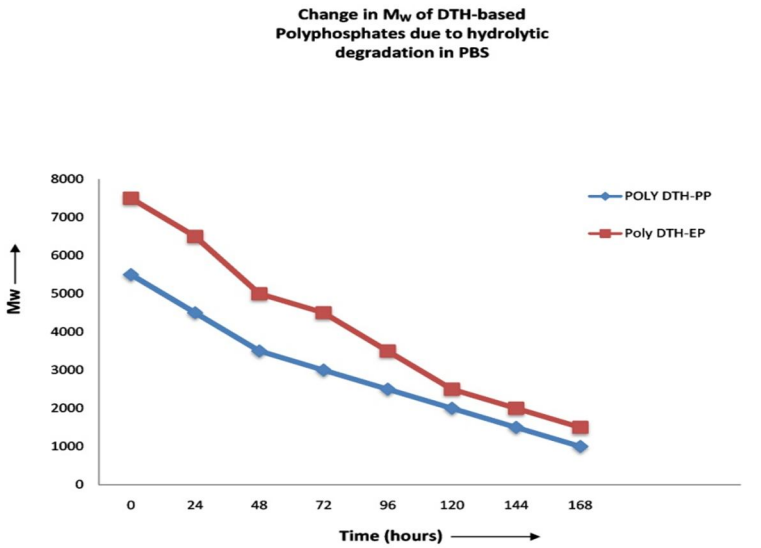


**Fig.2 Molecular weight loss data of hydrolytic degradation of E-tyrosine based polyphosphates due to hydrolytic degradation in PBS.**

*C. Degradation behavior of protein L-tyrosine based polyphospahtes on local pH :*

In this context of such reports, we considered to study the effect of degradation of protein *L*- tyrosine based polyphosphates as poly (DTH-EP) & poly (DTH-PP) pelletes on local pH range 6.23-7.4 at incubated physiological temp.of $37^0$ C and at a concentration of 15mg/ml with at specific time intervals over a period of 7 days (1 week), the pH of the supernant buffer is measured with a temp. corrected pH probe. In certain cases, these change in local pH has pronounced effect/ behavior on the actual performance of the biomaterial device as to tissue response of the body. For example, it has been reported that the acidic degredation products of the conventional polyster biomaterial like PLA, PGA, PCL etc and their co-polymer have adverse non-specific inflamatory effect in physiological environments especially in osseous tissue. Hence, such adverse effect have been found to coinicide with the growth of polymer degradation and the lowering of pH due to acidic degradation products. In figure-3, the pH values have plotted against time, show that the comparison of the local pH change due to degradation of respective polymers, where the polyphasphates apparently did not seem to have a drastic effect on lowering of pH of the surrounding mediated from the intital value. The minimum pH 6.23 value range signifie that these polymer do indeed release acidic degradation product, in form of phosphoric acid ($H_3PO_4$) derivatives. These current study of matters have the possibility of drop in pH value over one weak indicate that protein (*L*-tyrosine) based polyphosphates as biodegradable materials[11].

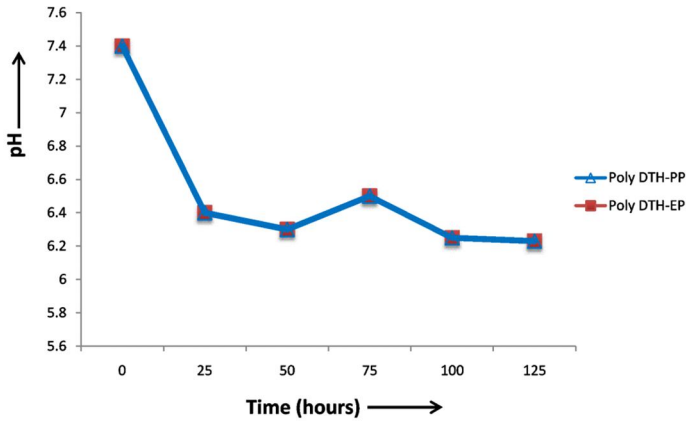


**Fig.3 Effect of L-tyrosine based polyphosphate polymer degradation on local pH: comparison between poly DTH-EP and Poly DTH-PP**

## III. CONCLUSION

In the present article, we have reported to protein (*L*-tyrosine) based polyphosphates and their potential bio-material application as bio-medical & engineering properties with predominately degradation characteristics[12]. The chemical solubility, hydrophilicity, hydrolytic degradability & their effect on local pH were studied for this purposes. The *L*-tyrosine based polyphosphates are found to be hydrophilic in nature as soluble in a variety of common organic solvents with chemical processability and hydrolytically degradable, to products, where, on comparison to pure poly (*L*-tyrosine) which is mainly insoluble & hardly degradable have improvement. Hence, by developing of potentially biodegradable novel polymeric biomaterials from naturally occurring poly *L*-amino acid, the *L*-tyrosine based poly phosphates hold significant promise to biomedical and bioengineering value now a day.

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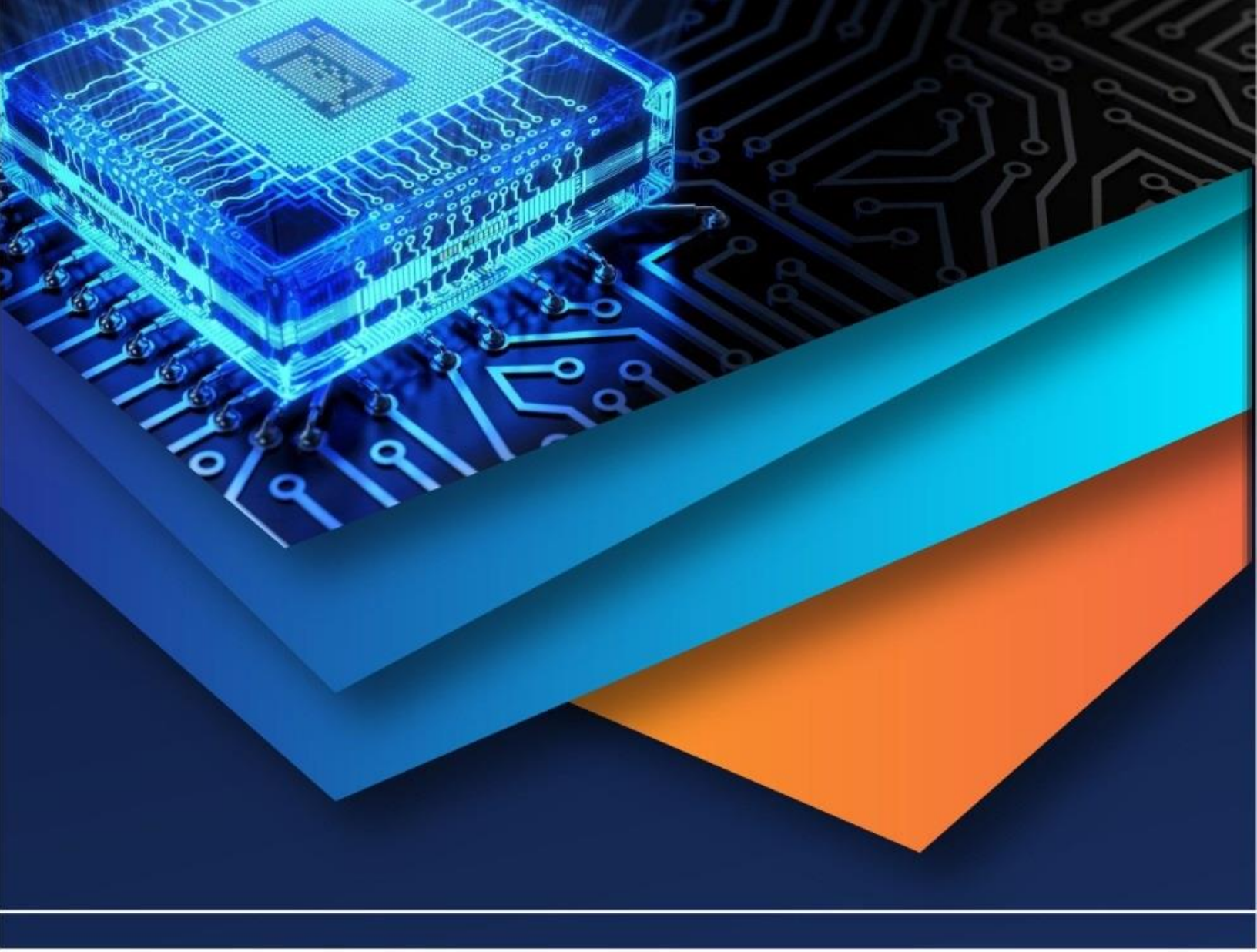

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