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# Structural and binding site Analysis and comparison between the Cyclooxygenase 1& 2 for inflammation and cancer diseases.

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***Abstract:** The inflammatory response in our body involves a catalyst, Cox (COX), that's liable for the formation of prostanoids. The 3 main teams of prostanoids --prostaglandins, prostacyclins, and thromboxanes square measure key components of however inflammation develops. There square measure 2 cyclo-oxygenase enzymes, one predominating at sites of inflammation (COX-2) and one constitutively expressed within the duct (COX-1), has LED to the vital therapeutic development of Cox inhibitors. we'll analyze the H bonds energy, Vdw forces and Fitness between the proteins and Legends. we'll perform all molecular modeling studies together with energy calculations, gradient, molecular dynamics simulations for all Legends, B-octylglucoside, N-acetyl-D-glucosamine, Rofecoxib and Alpha-D-mannose. Functional analysis are performed between cox one and cox2 proteins.*
***Keywords:** Cyclooxygenase, B-octylglucoside, N-acetyl-D-glucosamine, Rofecoxib and Alpha-D-mannose.*

## I. INTRODUCTION

### *A.* Cyclooxygenase (COX)

Cyclooxygenase (COX), formally said as prostaglandin-end peroxide syntheses (PTGS), is associate catalyst(EC one.14.99.1) that's formation of prostanoids, any as thromboxane and prostaglandins like prostacyclins.COX can be a target for medication meshed toward relieving inflammation, but by inhibiting COX these medication can have unwanted aspect effects.

### *B. Two Forms of Cyclooxygenase (COX)*

In the Nineties, researchers discovered different COX enzymes existed, currently called cyclooxygenase-1 and Cox-2. Cox (COX-1) is understood to be gift in most tissues. within the canal, cyclooxygenase-1 maintains the traditional lining of the abdomen. The protein is additionally concerned in excretory organ and thrombolytic operate. Cox-2 (COX-2) is primarily gift at sites of inflammation.

whereas every Cox-2 convert arachidonic acid to autacoids, resulting in pain and inflammation, their different functions produce inhibition of Cox-1 undesirable whereas inhibition of Cox is taken under consideration fascinating. but this is often not the only real action of the assorted forms of COX, that unit of measurement involved in many ancient cellular processes.

In terms of their life science, Cox-1 and Cox unit of measurement of comparable relative molecular mass, near to seventy and seventy 2 kDa, severally, and having sixty fifth amino alkanoic acid sequence similarity and near-identical action sites. the foremost very important distinction between the isoenzymes, that permits for selective inhibition, is that the substitution of essential compound at position 523 in Cox-1 with essential organic compound in Cox. The smaller Val523residue in Cox permits access to a hydrophobic side-pocket inside the macromolecule (which Ile523 sterically hinders). Drug molecules, like DuP-697 and conjointly the coxibs derived from it, bind to this varied web site and unit of measurement thought of to be selective inhibitors of Cox.

### *C. Difference Between COX1 and COX2*

Different types of prostanoids is simply synthesized within the body by victimization associate accelerator named as cylcooxygenase(COX).these prostanoids as well as prostaglandins, prostacyclin and thromboxane square measure vital biological mediators that play crucial role within the development of pain and inflammation within the body. therefore it's attainable to induce relief from pain and inflammation by inhibiting the COX accelerator.

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There square measure 3 differing kinds of COX enzymes like COX1, COX2 and COX3. they're similar in several aspects and have some variations too. The distinction between COX1 and COX2 is printed below.

*D. Difference in Name:*

COX-1 is additionally known as as organic catalyst as a result of it's created by a cell underneath all sorts of physiological conditions. the quantity at that organic enzymes ar created stay constant while not regard of substrate concentration and physiological demand. On the opposite hand Cox is associate degree inducible catalyst because it is created underneath sure specific conditions like inflammation.

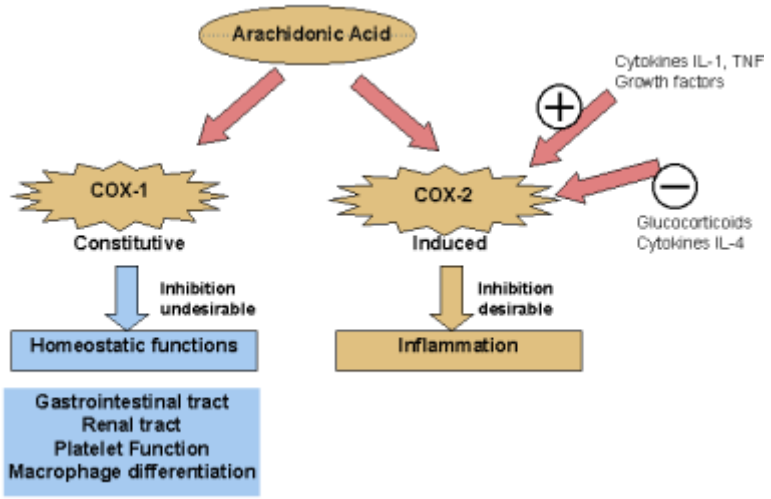
*E. Difference in Locations:*

COX-1 is often found within the excretory organ, abdomen and platelets whereas cyclooxygenase is found in macrophages, leukocytes and fibroblasts.

*F. Difference in Functions:*

COX-1 play necessary role in housework like it protects stomachal membrane, regulate stomachal acid and maintain traditional functions of the urinary organ by stimulating prostaglainds. cyclooxygenase-2 is concerned within the synthesis of prostaglandins that causes pain and inflammation within the body.

*G. Difference in Production:*




The stimulation of cyclooxygenase-1 accelerator is completed on endless basis by the body however Cox-2 accelerator didn't gift at traditional condition and created solely at the time of would like. The stimulation of Cox-2 enzymes relies upon cytokines.

*H. Difference in Usefulness:*

COX-1 enzymes square measure protecting in nature and so square measure helpful for the body. thus there's no got to inhibit them however Cox-2 enzymes play a very important role in inflammation and symptom. thus it's eager to inhibit Cox-2 enzymes.

*I. Difference in Inhibition:*

There are differing kinds of medicine that ar wont to inhibit cyclooxygenase-2 catalyst as well as Cox-2 inhibitor. Nonsteriodial antiinflammatoru medicine inhibit each cyclooxygenase-1 and cyclooxygenase-2 enzymes.

Cox (COX; autocoid G/H synthase, EC 1.14.99.1) catalyzes the primary 2 steps within the synthesis of prostaglandins (PGs). the 2 COX isoforms cyclooxygenase-1 and cyclooxygenase-2 ar the targets of the wide used anti-inflammatory medicine, indicating a task for these enzymes in pain, fever, inflammation, and tumorigenesis. the ever-present constitutional expression of cyclooxygenase-1 and inducible expression of cyclooxygenase-2 have crystal rectifier to the wide control belief that cyclooxygenase-1 produces physiological state PGs, whereas PGs made by cyclooxygenase-2 ar primarily pathophysiological.

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However, recent discoveries decision this paradigm into question and reveal so far underappreciated functions for each enzymes. This review focuses on a number of these new insights.

## II. CYCLOOXYGENASE LIGANDS

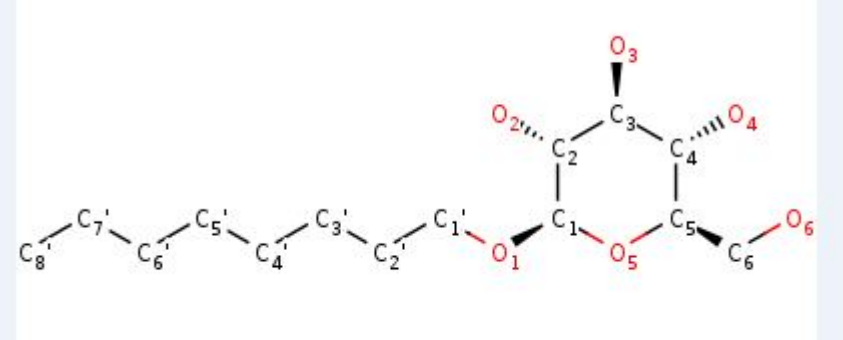
Cyclooxygenase ligands are devided into two types.They are cox1 ligands and cox2 ligands.

### *A. Cox1 ligands*

Prostaglandin endoperoxide H synthases (PGHSs)-1 catalyze the committed step in prostaglandin biosynthesis. Both isoforms are targets of nonsteroidal antiinflammatory drugs (NSAIDs). PGHSs area unit homodimers that exhibit half-of-sites COX activity; what is more, some NSAIDs cause accelerator inhibition by binding just one compound. to find out a lot of concerning the cross-talk that has got to be occurring between the monomers comprising every PGHS-1 chemical compound, we tend to analyzed structures of PGHS-1 crystallized underneath totally different conditions as well as within the absence of any tightly binding substance and within the presence of nonspecific NSAIDs and of a cyclooxygenase-1 substance.examples for cox1 ligands area unit B-Octylglucoside and N-Acetyl-D-Glucosamine.

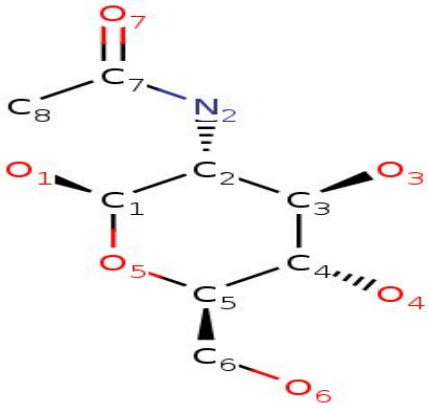
***1)*** *B-Octylglucoside*

$C_{14}\,H_{28}\,O_6$



***2)*** *N-Acetyl-D-Glucosamine*

$C_8\,H_{15}\,N\,O_6$



### *B.* **Cox2 ligands**

Rofecoxib (Vioxx) was one in every of the primary selective Cox (COX-2) inhibitors (coxibs) to be approved to be used in humans. Cox-2 {inhibitor} is exclusive therein the inhibitor contains a alkyl sulfone moiety in situ of the bactericide moiety found in different coxibs like Celebrex and valdecoxib. new crystallization conditions were acquainted that allowed the structural determination of human Cox in refined with Vioxx and to boot the structure was once determined to a pair of.7Å resolution. The crystal structure provides the primary atomic level details of the binding of Vioxx to Cox.

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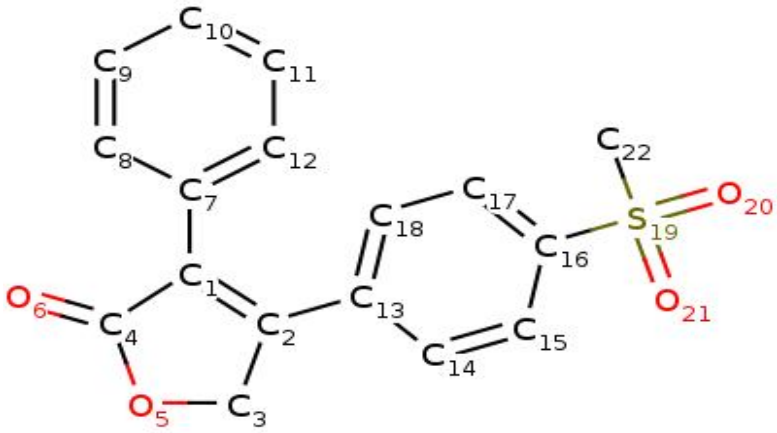
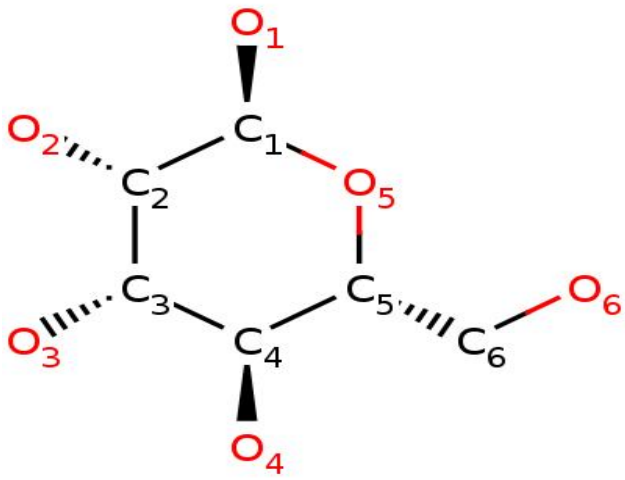
1) *Rofecoxib*
$C_{17}\,H_{14}\,O_4\,S$




2) *Alpha-D-Mannose*
$C_6\,H_{12}\,O_6$




## III. PROJECT RESULTS

*A. Hyer chem:*

HyperChem may be a molecular modelling and a robust procedure tool utilized in drug style. It offers many sorts of molecular and quantum physics calculations. improvement of little molecules in solvent and macromolecule advanced . By exploitation HyperChem we are able to style 3d structure of the Ligands. The intra molecular energies of matter-solvent and ligand macromolecule are going to be calculated exploitation molecular mechanics calculations of Hyperchem software package. Here we tend to ar conniving the energies and gradient of Ligands.

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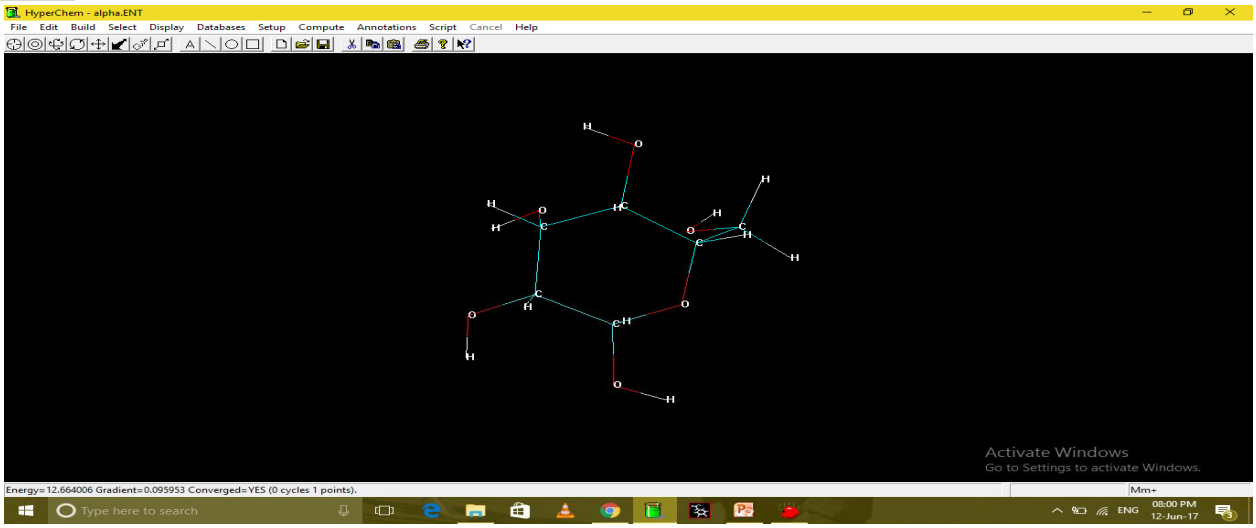

Fig1: Hyper chem output of alpha d mannose

Energies and Gradient of Ligands

| LIGANDS | ENERGY | GRADIENT |
|---|---|---|
| B octylglucoside | 21.8876 | 0.09711 |
| N acetyl D glucosamine | 18.6641 | 0.05066 |
| Rofecoxib | 28.24682 | 0.097408 |
| Alpha D mannose | 12.6640 | 0.09590 |

Table 1: Geometrical Optimization Of Ligands Using Hyperchem

### *B. Docking*

Docking could be a strategy that predicts the favored introduction of initial atom to an instant once sure to one another to form a stable complicated. Molecular arrival could be a machine technique to get proscribing strategies of ligands to their receptors speedily. Molecular communications assume the key half in each single organic response. The overwhelming majority of the organic responses get activated by authoritative of a bit sub-atomic matter to their receptor, that is mostly a supermolecule. Indeed, even the bigger a part of the medications apply their medical specialty responses rely simply upon their fruitful authoritative to their receptor's dynamic website within the body on these lines either imitating or analgesic the impact of traditional ligand's official to the receptor. we will find the coupling effinity/wellness of the substance with individual matter.

| LIGANDS | hb_ext | vdw_ext | hb_int | hb_ext |
|---|---|---|---|---|
| B-octylglucoside | 27.43 | 35.06 | 0.00 | -20.40 |
| N-acetyl-D-glucosamine | 20.10 | 50.09 | 0.00 | -65.96 |
| Rofecoxib | 11.23 | 19.62 | 0.00 | -4.75 |
| Alpha-D-mannose | 19.81 | 26.86 | 0.00 | -16.55 |

TABLE 2 : Strengths of Hydrogen Bonds and Vandewaals Bonds

### *C. Binding Energy*

From the above results we are calculating the binding energies between the Ligands and corresponding proteins by using the below stated formula.

Fitness = S(hb_ext) + 1.3750*S(vdw_ext) + S(hb_int) + 1.0000*S(hb_ext)

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| LIGANDS | FITNESS |
|---|---|
| B octylglucoside | 71.56 |
| N acetyl D glucosamine | 65.68 |
| Rofecoxib | 47.26 |
| Alpha D mannose | 49.18 |

TABLE 3: Binding energies between ligands and Proteins

## IV. CONCLUSION

We have used the following Ligands for Docking studies with proteins using Gold docking software. B-octylglucoside,N-acetyl-D-glucosamine,Rofecoxib and Alpha-D-mannose. We also performed the molecular modeling studies of Ligands including, 3d structure of cox enzymes, and energy minimization by using Hyperchem modeling software. Finally we docked those Ligands into the active site of proteins.Obtained the Binding energies of Ligands.

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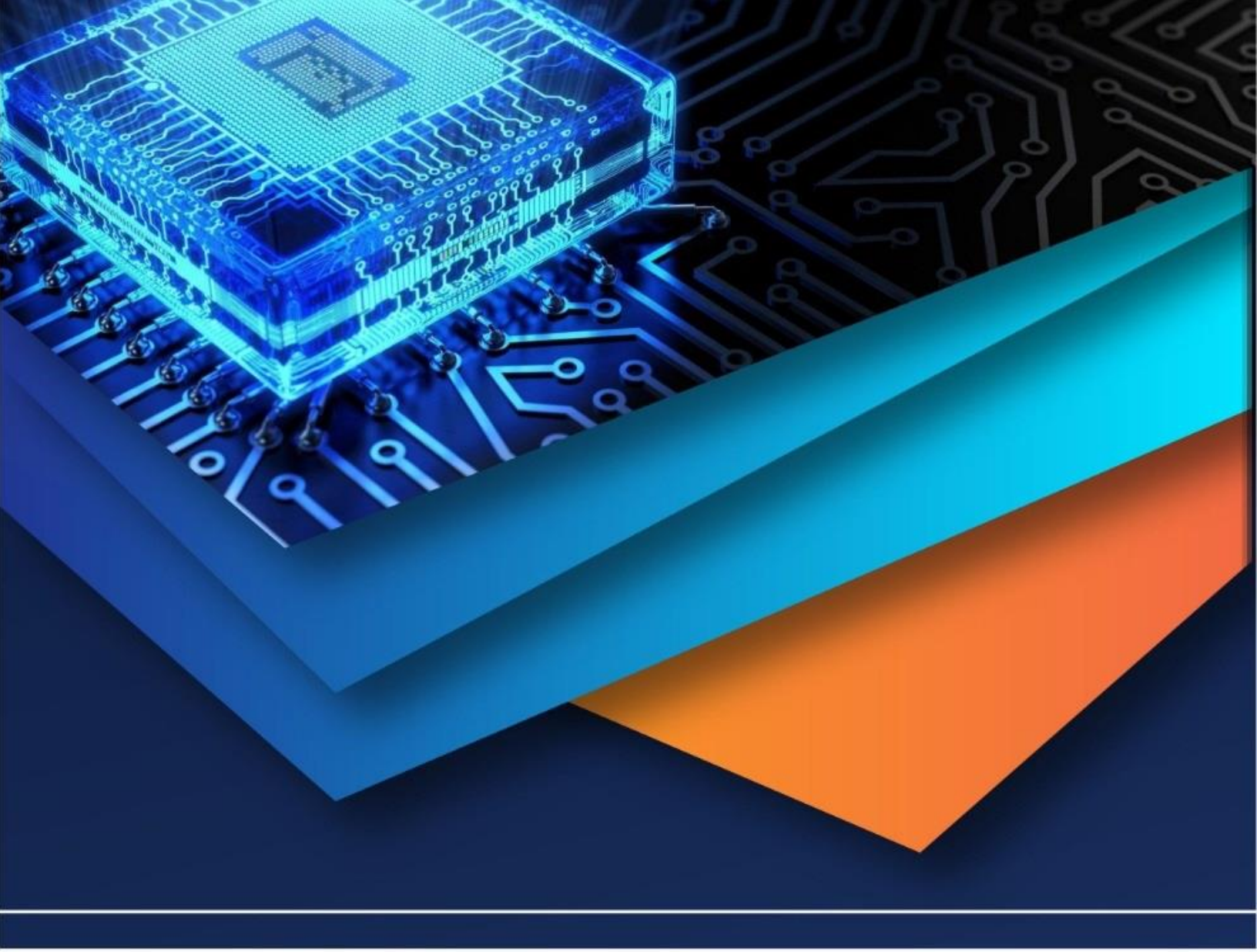

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