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Disease Target Identification and Validation of Alzheimers, Diabetes, Asthama and Arthiritis

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Abstract: Identifying the disease targets plays a important role for complex and multifactorial disease for which the mechanism is still not fully understood. As new insights into disease progression are discovered new drugs must be designed to target. Protein targets are identified for disease like Alzheimer's, Diabetes, Asthma and Arthritis .Target validation is a process by which we predict molecular target for the given protein and it also include identification of 3D structure. Protein targets will be identified for the given Target protein. Target proteins binding cavity or binding pockets will be identified and interaction studies will be performed.

Keywords: Alzheimer's, Diabetes, Asthma, Arthritis, Hyperchem,

I. INTRODUCTION

A. Alzheimer's disease

Alzheimer's disease is a neurological disorder which results in dementia. It causes problems like loss of memory, thinking and behavior. These symptoms develop slowly and progress gradually. Alzheimer's disease accounts for 60 to 80 percent of dementia cases. It is not a normal part of ageing but even 5 percent of people with the disease have early onset Alzheimer's.

B. Diabetes disease

Diabetes or Diabetes mellitus is a metabolic disease in which person has high blood sugar because insulin production is inadequate. complications linked to badly controlled diabetes are Heart problems , Hypertension and Mental health.

C. Asthma

Asthma is a chronic disease involving the airways in the lungs. These airways, or bronchial tubes, allow air to come in and out of the lungs.Asthma could be a disease poignant the airways that carry air to and from your lungs. those who suffer from this chronic condition (long-lasting or recurrent) square measure same to be wheezy. People who suffer from this chronic condition are said to be asthmatic.

D. Arthritis

Arthritis is very common. Actually, "arthritis" is not a single disease. It is an off-the-cuff means of relating joint pain or joint malady. Potential causes for inflammatory disease could include
Injury - leading to degenerative arthritis
Inheritance - such as in osteoarthritis
Abnormal metabolism

II. DISEASE PROTEIN TARGET AND DRUGS

A. Alzheimer's ailment protein target

D (2) DOPAMINE RECEPTOR D (2) Dopamine receptor is an ailment target protein for Alzheimer's
Ailment. It is additionally alluded as D2R. In people it is coded by qualities DRD2 The D2 receptor is known to interact with the D1 receptor and adenosine A2 receptor

B. Protein 3d Structure

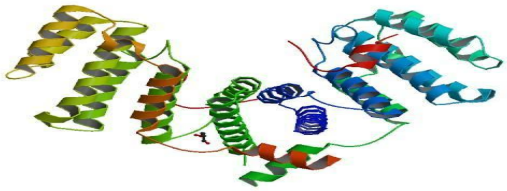

Fig1:3D Structure of D(2) Dopamine Receptor

C. Protein target binding site

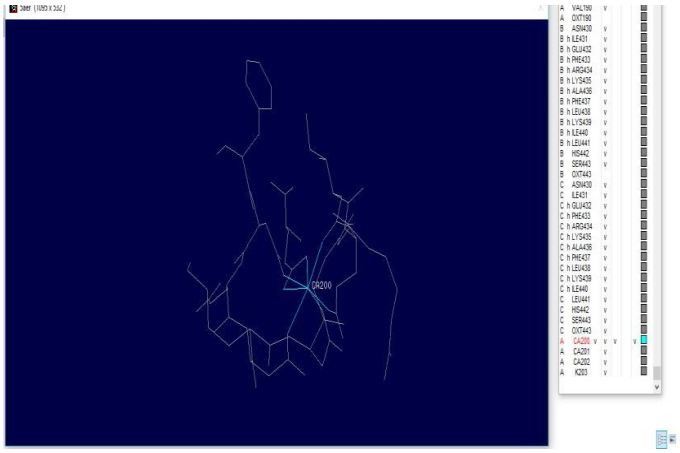

Fig2. Binding site of D(2) Dopamine Receptor is IYR36

Binding site of a D(2) Dopamine Receptor protein can be find by using Swiss pdb viewer. All the residues of the molecule or protein are found by opening the pdb file in the tool. Active site of the molecule can be identified my making heterogeneous residue of the active and remaining residues inactive and choosing the radius about 6 Armstrong .Then this site will be is the basic unit of active site.

D. Drug For Alzheimer's Disease: Loxopine

1) Drug structure

Fig 3: 2D Structure of the Loxopine.

E. Diabetes Aliment Protein Target: Lipoprotein Lipase

Lipoprotein lipase (LPL) is belonged to lipase gene family. It is a water soluble enzyme that hydrolyzes triglycerides. The Apolipoprotein APOC2, acts as a co substance of LPL activity within the presence of lipids on the purple heart surface of tube epithelial tissue.

1) Protein 3d structure

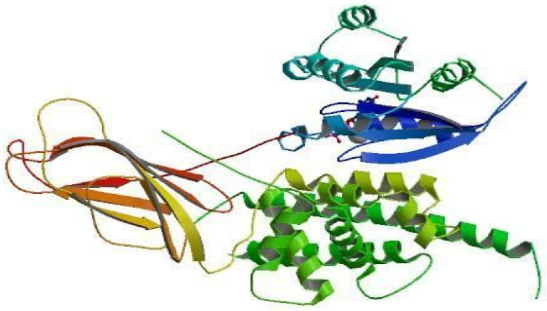

Fig 4: 3D Structure of Lipoprotein Lipase

2) Protein Target Binding Site

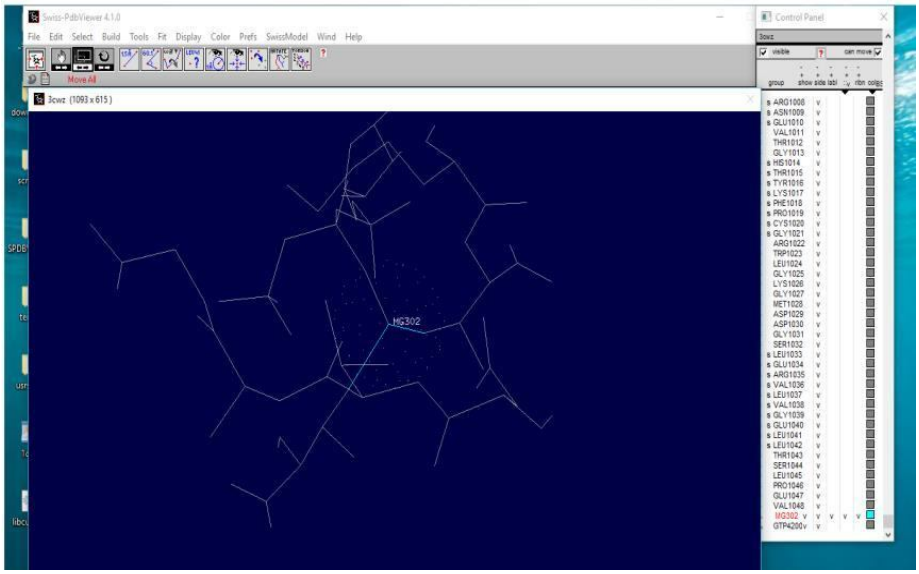

Fig 5: Binding site of Lipoprotein Lipase is COH601

Binding site of a Lipoprotein lipase protein can be find by using Swiss pdb viewer . All the residues of the molecule or protein are found by opening the pdb file in the tool .Active site of the molecule can be identified my making heterogeneous residue or A chain residue active and remaining residues inactive and choosing the radius about 6 Armstrong .Then this site will be is the basic unit of active site

F. Drug For Diabetes: Clofibrate

1) Drug structure

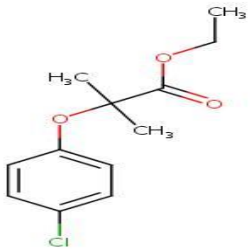

Fig 6: 2D Structure of Clofibrate

G. Asthma aliment protein target

ALPHA ADRENERGIC RECEPTOR Adrenaline is the epinephrine. Alpha adrenergic receptor is G protein coupled receptor. Activation of this protein produces epinephrine(E)(80%) and norepinephrine(NE)(20%). It activates Vascular smooth muscle, Mydriasis, Genitourinary tract smooth muscle.

H. Protein 3d structure

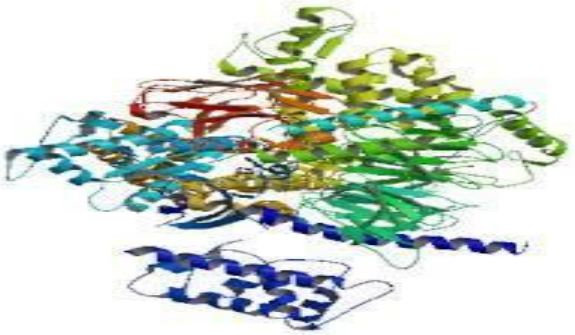

Fig7:3D Structure of Alpha Adrenergic Receptor.

I. Protein target binding site

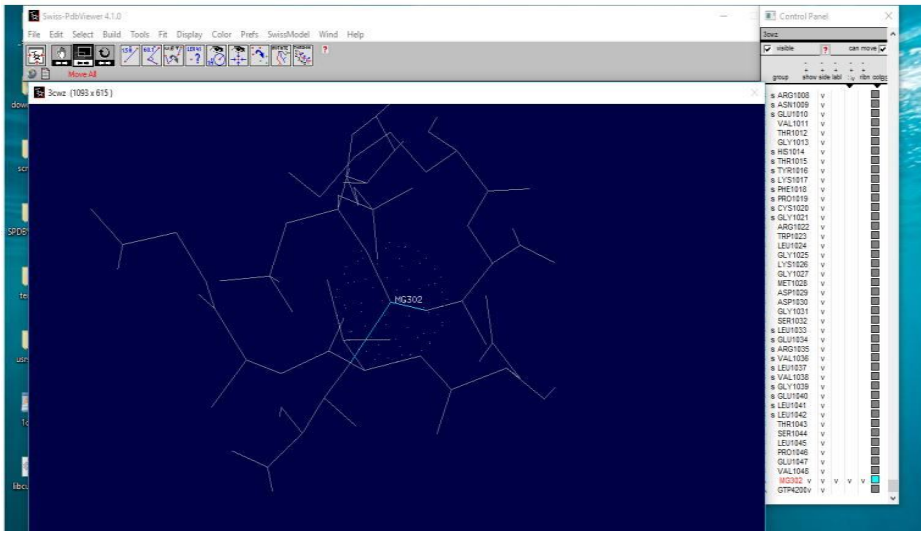

Fig 8:Binding site of Alpha Adrenergic Receptor is ALA101

Binding site of a Alpha Adrenergic Receptor protein can be find by using Swiss pdb viewer . All the residues of the molecule or protein are found by opening pdb file in the tool .Active site of the molecule can be identified my making heterogeneous residue or

A chain residue active and remaining residues inactive and choosing the radius about 6 Armstrong .Then this site will be is the basic unit of active site.

J. Drug For Asthma: Ephedrine

1) Drug structure

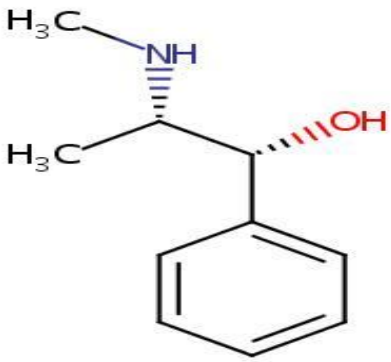

Fig 9:2D Structure of Ephedrine Drug.

K. Arthritis ailment protein target

CYCLOOXYGENESE Cyclooxygenease (COX) is often referred as prostaglandin-endoperoxide synthase that's chargeable for formation of prostanoids, as well as thromboxane and prostaglandins like prostacyclin

COX-1 activity is believed to be chargeable for manufacturing cytoprotective prostaglandins, like prostacyclin and PGE2, that square measure thought to be essential to keep up integrity of internal organ tissue layer.

1) Protein 3d structure

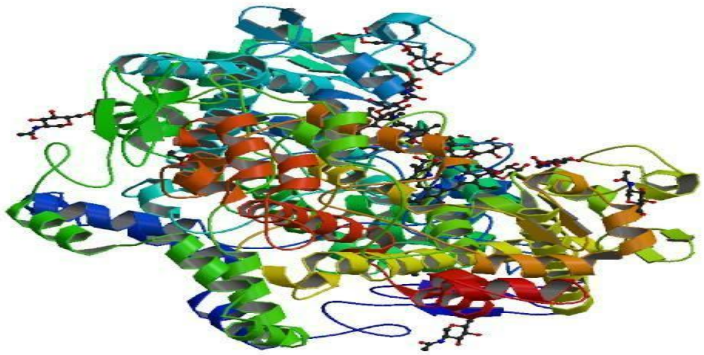

Fig 10:3D Structure of Cyclooxygenese protein .

L. Protein target biding site

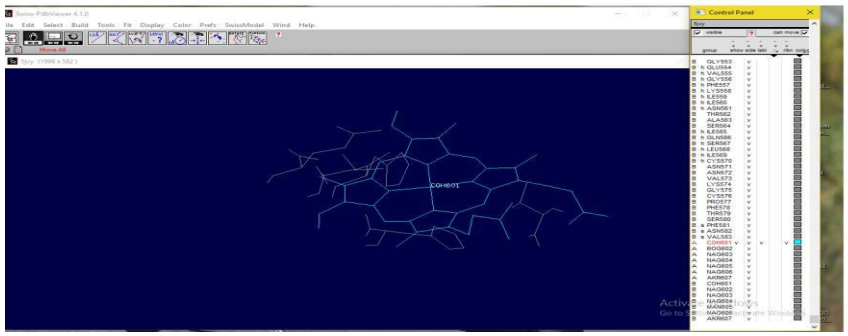

Fig 11:Binding site of Cyclooxygenese is MG302

Binding site of a Cyclooxygenese protein can be find by using Swiss pdb viewer . All the residues of the molecule or protein are found by opening pdb file in the tool .Active site of the molecule can be identified my making heterogeneous residue or A chain residue active and remaining residues inactive and choosing the radius about 6 Armstrong .Then this site will be is the basic unit of active site

M. Drug For Arthritis: Aspirin

1) Drug structure

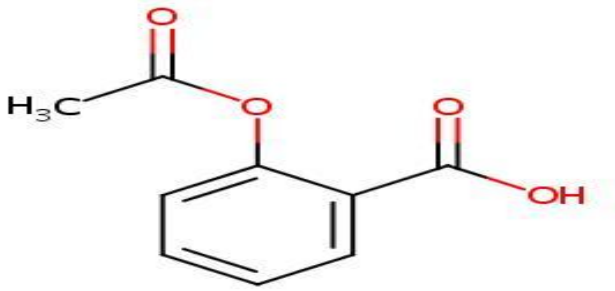

Fig12:2D Structure of Aspirin.

III. PROJECT RESULTS

A. PDB

Three Dimensional structure of protein can be retrieved using Protein data bank and protein binding sites can be identifies by using Swiss pdb viewer.

B. Hyer Chem

Hyper Chem is a molecular modelling and a powerful computational tool used in drug design. It offers many types of molecular and quantum mechanics calculations. Optimization of small molecules in solvent and protein complex By using Hyper Chem we can design 3d structure of the Inhibitor. The intra molecular energies of ligand-solvent and ligand protein will be calculated using molecular mechanics calculations of Hyper chem software. Here we are calculating the energies and gradient of Inhibitors.

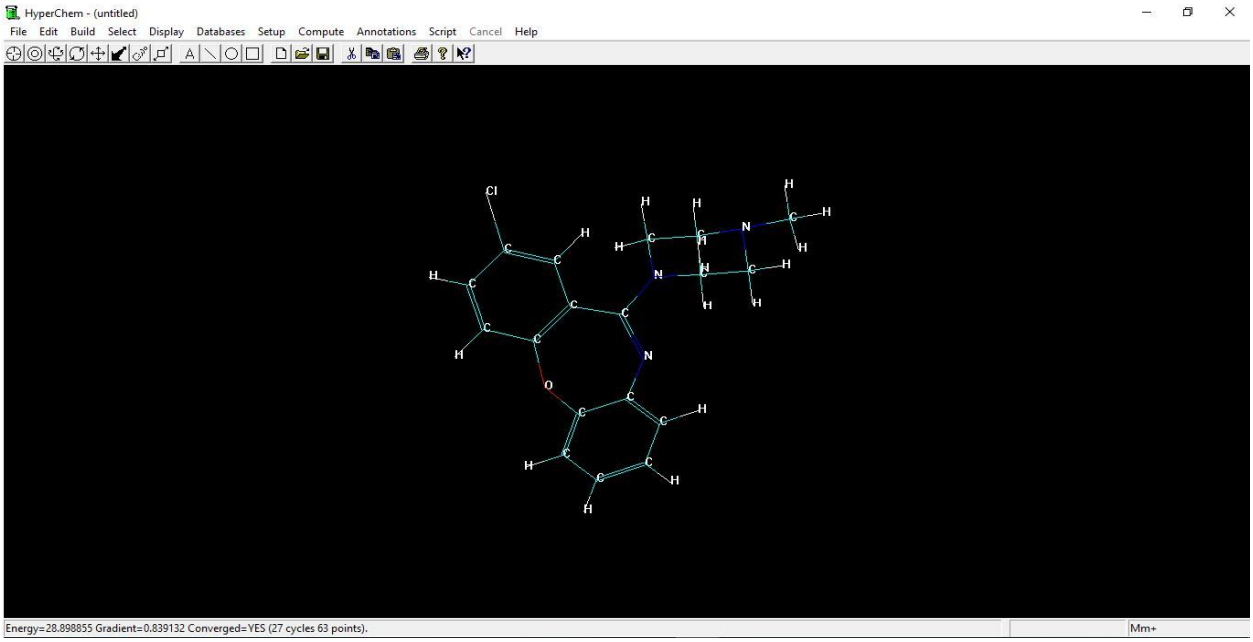

Fig 13:Hyper chem output of Loxopin.

C. Energies and gradient of drugs

DRUGS	ENERGY	GRADIENT
LOXOPINE	28.89	0.839
CLOFIBRATE	18.284	0.876
EPHEDRINE	20.386	0.768
ASPIRIN	14.37	0.0873

Table 1: Geometrical Optimization Of Drugs Using Hyperchem

D. Docking

Docking is a strategy which predicts the favored introduction of first atom to a moment when bound to each other to shape a stable complex. Molecular Docking is a computational technique to discover restricting methods of ligands to their receptors rapidly. Molecular communications assume the key part in every single organic response. The vast majority of the organic responses get activated by authoritative of a little sub-atomic ligand to their receptor, which is generally a protein. Indeed, even the greater part of the medications apply their pharmacological responses depend just upon their fruitful authoritative to their receptor's dynamic site inside the body along these lines either imitating or moderating the impact of normal ligand's official to the receptor. We can locate the coupling effinity/wellness of the inhibitor with individual ligand.

DRUG	PROTEIN	S(hb_ext)	S(vdw_ext)	S(hb_int)	S(Vdw_int)
Loxopine	D(2)Dopamine Receptor	14.55	0.23	0.00	-14.66
Clofibrate	Lipoprotein Lipase	1.31	-12.90	0.00	-80.34
Ephedrine	Alpha Adrenergic Receptor	0.03	36.25	0.00	-56.51
Aspirin	Cyclooxygenease	7.51	48.15	0.00	-21.94

TABLE 2 : Strengths of Hydrogen Bonds and vanderwall bonds

E. Binding Energy

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

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

Drug	Protein	Fitness
Loxopine	D(2)Dopamine Receptor	0.20
Clofibrate	Lipoprotein Lipase	-96.76
Ephedrine	Alpha Adrenergic receptor	-6.63
Aspirin	Cyclooxygenease	51.76

TABLE 3: Binding energies between Drugs and Proteins

IV. CONCLUSION

Protein targets are identified for the disease like Alzheimer's, Diabetes, Asthma and Arthritis. Target validation of the protein for corresponding disease which include 3D structure, identification of drugs and inhibitors are identified and interaction studies are performed. It also includes the identifying the binding site by using the Swiss pdb viewer.

Molecular modeling studies of drugs including energy minimization, identification of gradient for the drug by using hyperchem are performed. Docking the target protein with the conserved drug with minimum energy of the corresponding active binding site of the proteins are performed by using the gold docking software.

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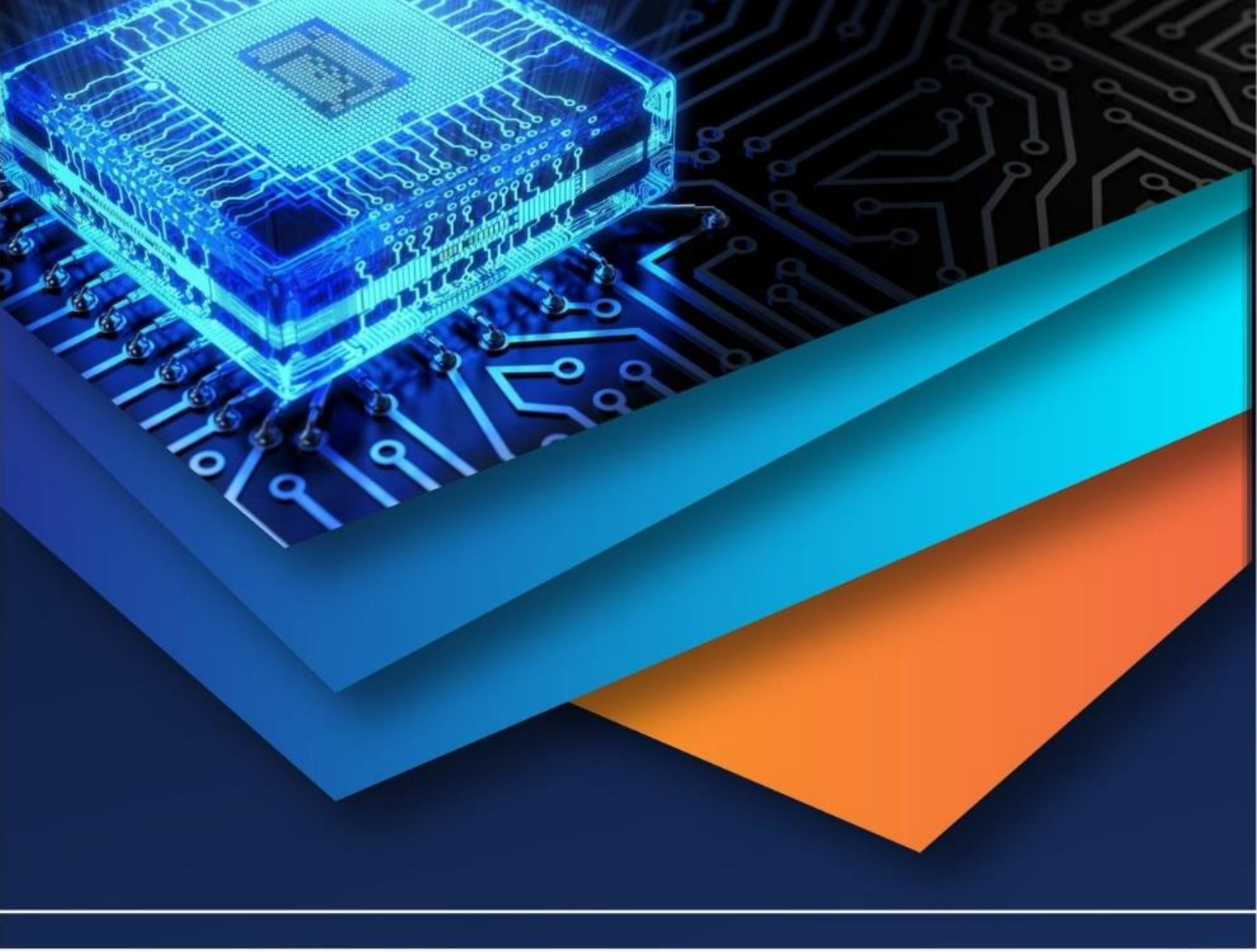

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