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DOCKING STUDY OF FLT3 RECEPTOR WITH TYROSINE KINASE FOR LEUKEMIA DISEASE

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Keywords:

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ABSTRACT: Leukemia is a disease of cancer that affects blood-forming tissues *i.e.,* bone marrow and lymph nodes, which is associated with uncontrolled growth of WBCs. These cells are unable to fight against infection and weaken the ability of bone marrow to make RBCs and platelets. When leukemic cells overproduce, they interfere in circulatory cells' functioning, *i.e.,* RBCs and platelets. Along this, leukemia's pathogenesis is unique in relation to different malignant growths which ordinarily start in major organs and then spread in bone marrow. Different types of leukemia are discovered based on different classification systems with the two major leukemia types - acute and chronic. The work includes the 50-year history of leukemia-lymphoma cell lines, which is considered a key model system in biomedicine. The work involves finding suitable protein receptors for the available potent drugs. Protein receptors are the target sites where drug molecules bind, activate and start their response. FLT3 tyrosine kinase protein is taken as a receptor to study docking concerning ligands like Abacavir, Gabapentin, *etc*. Autodock and Discovery Studio were used based on which best binding energy of Abacavir was found to be -7.31.

INTRODUCTION: Leukemia is a cancer of blood-forming tissues which includes bone marrow and lymphatic system. It involves the white blood cells, which are called Leukocytes. These cells are infectious fighters. They grow normally and divide in an orderly manner as our body needs them. But the rapid production of abnormal white blood cells in blood and bone marrow results in cancer which is called leukemia. These cells are unable to fight against infection and weaken the ability of bone marrow to make red blood cells and platelets.

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When leukemic cells overproduce, they interfere in the functioning of several other circulatory cells, *i.e.,* red blood cells (erythrocytes) and platelets. Thus, also affect bone marrow and then goes into the bloodstream, also conquer lymph nodes, spleen, liver, and central peripheral nervous system. Along this, leukemia's pathogenesis is unique in relation to different malignant growths which ordinarily start in major organs and then spread in the bone marrow [1, 2, 3].

How Does Leukemia Develop?

How Does Leukemia Effect the Body: It begins in the developing cells in the bone marrow. All these cells start the process of haemopoiesis, which results in the heamopoitic cells (hemo=blood, poiesis= make). These stem cells grow in multiple development stages until they reach adulthood.

These blood cells develop into myeloid cells or lymphoid cells. The mature forms of these cells are myeloid cells which mature into red blood cells, platelets, and white blood cells such as basophils, neutrophils, and eosinophils). Lymphoid cells mature into white blood cells (lymphocytes and natural killer cells) [4].

History: There is an almost 50-year history of leukemia-lymphoma (LL) cell lines - a key model framework in biomedicine. Because of the point-by-point documentation of their oncogenomic and transcriptional adjustments using late advances in sub-atomic medication, LL cell lines might be fitted to parent tumors with a level of accuracy unreachable in different diseases. Based on literature survey, we have overviewed the corpus of distributed LL cell lines and discovered 637 models that satisfy the least guidelines of confirmation and portrayal. Even though cell lines speak to the principle of hematopoietic formative cell types, some LL classifications determinedly oppose foundation *in-vitro*. The appearance of building methods for deifying essential human cells that keep up separation implies now is the ideal opportunity for restored scan for *in-vitro* models from underrepresented hematologic substances. Given their complex applications in biomedicine, there is little uncertainty that LL-inferred cell lines will keep on having a crucial influence well into the following 50 years also [5].

Statistics: Leukemia is most prevalent among whites and least among American Indians/Alaskan locals. The occurrence of leukemia ranges between 10-18 for every 100,000 person worldwide with a little male predominance, while, the death rate is 5-9 for every 100,000 yearly. The frequency pace of youth leukemia shifts globally, between 0.4-4 for every 100,000 every year, with the most reduced rates being recorded in dark African youngsters. Leukemia can be intense or ceaseless and Lymphocytic or Myelogenous.

It happens most generally in grown-ups over 55 years and kids more youthful than 15 years. The treatment techniques rely upon the platelet influence and whether the leukemia is intense or incessant or Lymphocytic or Myelogenous. Chemotherapy is much of the time used to treat leukemia [5].

Pace of New Cases and Deaths per 100,000: The pace of new instances of leukemia was 14.1 per 100,000 people every year. The demise rate was 6.4 per 100,000 people every year. These rates are age-balanced and dependent on 2013–2017 cases and passing. Lifetime Risk of Developing Cancer: Approximately 1.5 percent of people will be determined to have leukemia sooner or later during their lifetime, in light of 2015–2017 information. The pervasiveness of This Cancer: In 2018, there were an expected 459,048 individuals living with leukemia in the United States.

In India, every year >10,000 instances of youth leukemia have been accounted for all, representing 60 to 85% of all youth leukemias. The frequency of leukemia in the Indian pediatric populace was 34%, of which 25% was ALL [6]. Regardless of the presence of a national library for kid hood leukemia, difficulties, for example, under-announcing because of the absence of mindfulness, under-finding, and lacking framework despite everything existing, which add to the scarcity of precise information, delay in perceiving the infection on schedule and a late referral. This can put the youngster in a high-hazard classification. Thus, improved mindfulness among the doctors, medicinal services suppliers, and the overall population is basic.

Classification of Leukemias: The four most common types of leukemia are: Acute lymphocytic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, and chronic myeloid leukemia

Acute Lymphocytic Leukemia: This is a cancer of blood and bone marrow. “Acute” in acute lymphocytic leukemia originates from the fact that the disease grows quickly and makes juvenile platelets, as opposed to developing ones. “Lymphocytic” in acute lymphocytic leukemia refers to the white blood cells called lymphocytes, which ALL affects. Acute lymphocytic leukemia is also known as acute lymphoblastic leukemia. The primary treatment for ALL is Chemotherapy [7]. Intense lymphocytic leukemia is the most widely recognized malignancy in youngsters, and medicines give a decent possibility for a fix. Intense lymphocytic leukemia can likewise happen

in grown-ups; however, the possibility of a fix is enormously decreased.

Acute Myeloid Leukemia: AML called acute non-lymphocytic leukemia, starts in the bone marrow and moves into the blood, and spreads into the other body parts, which includes the lymph nodes, liver, spleen, central nervous system(brain and spinal cord), and testicles. Acute myeloid leukemia (AML) has many other names, including acute myelocytic leukemia, acute myelogenous leukemia, acute granulocytic leukemia, and acute non-lymphocytic leukemia. Acute myeloid leukemia is brought about by harm to the DNA of creating cells in your bone marrow. At the point when this occurs, platelet creation turns out badly. The bone marrow produces youthful cells that form into leukemic white platelets called myeloblasts. These strange cells can't work appropriately and can develop and swarm out sound cells. Much of the time, it's not satisfactory what causes the DNA transformations that lead to leukemia. Radiation, presentation to specific synthetic concoctions and some chemotherapy drugs are realized hazard factors for intense myelogenous leukemia [8].

Chronic Lymphocytic Leukemia: Chronic Lymphocytic leukemia is a type of cancer in which myelogenous leukemia is brought about by harm to the DNA of creating cells in your bone marrow. At the point when this occurs, platelet creation turns out badly. The bone marrow produces youthful cells that form into leukemic white platelets called myeloblasts. These strange cells can't work appropriately and can develop and swarm out sound cells.

Much of the time, it's not satisfactory what causes the DNA transformations that lead to leukemia. Radiation, presentation to specific synthetic concoctions and some chemotherapy drugs are realized hazard factors for intense myelogenous leukemia. The immature-incompetent, self-renewing B cells accumulate enormously because of faulty apoptosis mechanisms. It originates from antigen-stimulated mature B lymphocytes plenish by proliferating precursor cells. It may not cause any symptoms for years but if occur, it includes swollen lymph nodes and fatigue. Lymphocytic leukemia most regularly influences more older adults [9].

Chronic Myeloid Leukemia: CML is a myeloproliferative, immature microorganism issue described by clonal extension of a crude pluripotent undifferentiated cell that can separate into the myeloid, monocyte, megakaryocyte, and erythrocyte ancestries. CML is related to complementary movement between chromosome 9 and 22. This chromosomal variation from the norm is generally alluded to as Philadelphia (Ph) chromosome. The chromosomal movement in the Ph issue is related to the fundamental encoding of combination proteins displaying tyrosine kinase action. This raised articulation of tyrosine kinase prompts uncontrolled cell development [10].

Causes of Leukemia: Few of the causes of leukemia are as follows:

Down Syndrome: ALL is a harmful change and multiplication of lymphoid forebear cells in the bone marrow, blood, and extramedullary locales. While 80% of ALL happens in youngsters, it speaks to an overwhelming infection when it happens in grown-ups.

Chemotherapy/Radiation: Being treated for another disease with chemotherapy or radiation can likewise put you at a higher hazard for leukemia later on. That is because DNA harm in early white platelets during chemotherapy can prompt leukemia DNA harm in early white platelets during chemotherapy can prompt leukemia entertainer for ALL and Chronic myelogenous leukemia (CML).

Inherited genetic disorders: Some uncommon acquired hereditary issues, for example, Bloom's condition, can be related to leukemia.

Smoking: Smoking cigarettes can expand the danger of creating AML. There is benzene in tobacco smoke, which will probably be a noteworthy reason. The danger of AML increments with the more cigarettes you smoke every day and the quantity of years you smoke.

Exposure to Benzene: Those who work at places that are exposed to Benzene at manufacturing jobs are found to be at risk.

Side Effects of Medication after Organ Transplant: Patients who have undergone organ

transplants, their immunity decreases and thus are at higher risk for leukemia.

Advanced Age: People who are older or more than 60 years of age are at more risk of leukemia [11].

Tests to Identify Human Leukemia: If someone has signs or symptoms, then he/she should go for the following tests:

Physical Examination: Physical signs will be observed by the doctor, like pale skin (Anemia), swelling in lymph nodes, and enlargement of the liver & spleen.

Blood Tests: By taking a sample of patients' blood, the doctor can decide whether patients have anomalous degrees of white platelets or platelets which may recommend leukemia.

Bone Marrow Tests: The doctor may prescribe a methodology to expel an example of bone marrow from your hipbone. The bone marrow is evacuated utilizing a long, dainty needle. The example is sent to a lab to search for leukemia cells. Specific trial of your leukemia cells may uncover certain qualities that are utilized to decide your treatment alternatives.

Chest X-beams: Chest X-beams helps to see whether leukemia or disease is the reason for lung issues, for example, diligent coughing or inconvenience relaxing.

CT Scan: CT scan of the head, chest, and gut helps to see whether leukemia has spread there or not.

Lumbar Puncture: Lumbar puncture is done to see whether leukemia cells are in your cerebrospinal.

MRI: MRI of the brain is done to investigate manifestations, for example, disarray, loss of motion, deadness, vision issues, vertigo, or cerebral pains. Those indications could imply that leukemia has spread to the cerebrum.

Biopsy: Biopsy of lymph nodes in different tissues helps to search for leukemia.

MATERIAL AND METHODS:

Role of Flt3 Receptor Tyrosine Kinase as a Drug Target in Leukemia: Flt3 (Flk2, STK1) is a hematopoietic receptor tyrosine kinase (RTK) that has been a lot of interest lately as a potential drug candidate. In acute myeloid leukemia, activation of Flt3 by one-of-a-kind mutations is needed for proliferation, apoptosis tolerance, and the prevention of leukemic blast differentiation (AML). In such mutation, internal tandems repeat replication within the Flt3 juxta membrane region has been connected to a poor prognosis. Changes in signaling, such as a completely suggested activation of STAT5, are caused by Flt3 remodeling, which leads to changes in the expression of gene profiles and cell transformation. Flt3 tyrosine kinase inhibitors' activity can be used to prevent excessive Flt3 signaling.

The phenyl-aminopyrimidine STI571 (Gleevec, Imatinib) is an important regulator of RTKs of the family, including the c-package, but Flt3 is resistant to it. The phenylalanine 691 side-chain in the ATP binding center prevents STI571 from binding to Flt3, and replacing it with threonine leaves the related Flt3 mutant vulnerable to STI571. They demonstrate distinct selectivity profiles for various kinases, between wild type and active Flt3, and between wild type and active Flt3. These compounds can potentially be used as experimental anti-AML drugs and probes for the signaling processes and pathways of the elegance III RTK family.

Flt3 controls the development and formation of hematopoietic cells and is represented myeloid and lymphoid progenitor cells. The Flt3 ligand, a monomeric polypeptide of around 200 amino acid residues, activates Flt3. FLT3 variations exist in one to three percent of newly diagnosed acute myeloid leukemia patients. This is a hematopoietic progenitor cell malignancy with a multitude of scientific pathways; the prevalence is more than double that of patients with chronic myelogenous leukemia (20,000 vs. 8500 new patients in step with yr., respectively, inside the USA).

Internal tandem duplication (ITD) in FLT3 is affected by a top-to-tail duplication of one to more than one hundred amino acids in the juxta membrane domain, which occurs in around 20%–25% of patients with acute myelogenous leukemias. Five to ten percent of these patients have FLT3 tyrosine kinase (FLT3 TK) mutations, usually located in the activation region.

Daunorubicin and idarubicin, as well as cytarabine, are the mainstays in the treatment of acute myelogenous leukemias. People over 50 who are not eligible for traditional therapy are typically given five-azacitidine, decitabine, or clofarabine. According to current medical studies, adding orally effective small molecule Flt3 inhibitors to such therapies can even improve the number of occasions-free and total life spans. Midostaurin has been licensed by the US Food and Drug Administration (FDA) for use in acute myelogenous leukemias with FLT3-positive mutations in combination with general cytarabine and daunorubicin for first-line induction chemotherapy and in combination with cytarabine for second-line consolidation chemotherapy. Gilteritinib is an Flt3 multikinase inhibitor that the FDA has licensed for the treatment of relapsed or refractory acute myelogenous leukemia in adults with FLT3 mutations.

Quizartinib is an Flt3 multikinase inhibitor that has been authorized by the Japanese Ministry of Health, Labor, and Welfare (MHLW) for the care of adults with relapsed or refractory Flt3-fantastic acute myelogenous leukemias. Kind II inhibitors include gilteritinib and quizartinib, both of which bind to Flt3 through the inactive DFG-Dout structure. Additionally, ponatinib is a multikinase inhibitor licensed for treating Philadelphia chromosome-positive acute lymphoblastic and chronic myelogenous leukemias; however, it is often used off-label to treat patients with acute myelogenous leukemia.

The FDA has licensed sorafenib for treating hepatocellular, renal cell, and discrete thyroid tumors and off-label usage in treating acute myelogenous leukemias during allogeneic hematopoietic stem cell transplantation. Sunitinib, crenolanib, FF10101, and lestaurtinib are only a handful of the other tablets actually being studied in clinical trials for this condition. Acute myelogenous leukemia, unlike chronic myelogenous leukemias, which are triggered solely by the development of the BCR-Abl chimeric protein kinase, may be caused by a multitude of causes and are likely to be immune to both cytotoxic and oriented healing therapies. As a result, a greater understanding of the etiologies of acute myelogenous leukemias and the advancement of more successful therapies could be needed immediately.

Mechanism of How FLT3 Cause Leukemia:

- At least one type of mutation causes activation of Flt3 receptor.
- For Flt3 signal transduction, many conserved pathways must be enabled, signaling cascades.
- This result in altered signaling.
- As a result of this, altered gene expression patterns and cell transformation arise.
- This finally may result in proliferation leukocytes *i.e.,* leukemia.

Databases Used:

DDBJ: It gives the services & analysis of nucleotide sequence data and supercomputer system to support research.

Gene Cards: It's a searchable, integrative database that allows you access to all annotated and projected human genes in a user-friendly format. The knowledgebase pulls gene-centric data from over 150 separate websites, including genomic, transcriptomic, proteomic, genetic, clinical, and practical data.

InterPro: It divides proteins into families and estimates their territories and positions, enabling researchers to examine their roles. Signatures and mathematical models are used in the process.

PIR: It's a public bioinformatics resource that supports researchers and scientists with genomic, proteomic, and systems biology study and studies.

RCSB PDB: This resource is powered by the Protein Data Bank archive-information about the 3D shapes of proteins, nucleic acids, and a complex assembly that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease [12].

PDBsum: A pictorial database that provides an at-a-glance overview of the contents of each 3D structure deposited in the Protein Data Bank (PDB). There are two types of searches text and Sequence searches. Information shown on PDBsum

pages are Top page, protein, DNA/RNA, Ligands, Prot-Prot, clefts and Links [13].

KEGG Pathway Data Base: KEGG (Kyoto Encyclopedia of Genes and Genomes) is a database resource that integrates genomic, chemical and systemic functional information. In particular, gene catalogs from completely sequenced genomes are linked to higher-level systemic functions of the cell. It is widely used as a knowledge base for integration and interpretation datasets which are processed by genome sequencing and other high experimental technologies. KEGG has expanded more applications on human diseases, drugs *etc* [14].

Zinc Data Bases: It is commercially available compound for structure based virtual screening. Currently it has 90 million purchased compounds, which is ready to dock. It is free for everyone and can easily be downloaded from the website. ZINC15 is in the process of being released as a new version of ZINC. The prior version was ZINC12 [15].

Drug Bank Data Base: This database is a comprehensive, freely accessible, online database containing information on drugs and drug targets. The latest release of the database (version 4.0) contains 7677 drug entries including 1558 FDA-approved small molecule drugs, 155 FDA-approved biotech (protein/peptide) drugs, 87 nutraceuticals and over 6000 experimental drugs. Its entry contains more than 200 fields in which half of the information is of the drug and half of the drug target. HMDB, T3DB, SMPD and FooDB are also part of a general suite of metabolomic/ cheminformatics databases [16].

Binding Databases: It is a public, web accessible database of binding affinities that focuses on interaction of proteins considered drug-targets with small, drug-like molecules. Binding DB contains 1,908,553 binding data, for 7,605 protein targets and 846,857 small molecules. The large and growing body of experimental data on molecular binding is of enormous value in biology, pharmacology, and chemistry. Applications include the assignment of function to biomolecules, drug discovery, molecular modeling, and nanotechnology. However, binding data are difficult to find and access because they are available almost exclusively through scientific journals [17].

PubChem: PubChem is a database of chemical molecules and their exercises against natural tests. The framework is kept up by the National Center for Biotechnology Information (NCBI), a segment of the National Library of Medicine, which is a piece of the United States National Institutes of Health (NIH) [18].

Uniprot: It contains the sequence of the protein as well as details about its role. It also serves as a data repository for annotations.

There is a list of drugs and ligands used. A list of Drugs used in leukemia is given in **Table 1** and list of Ligands given in **Table 2.**

TABLE 1: LIST OF DRUGS USED IN LEUKEMIA

S. no.	Drug Name	Uses
1	Imatinib	A tyrosine kinase inhibitor is a type of cancer growth suppressant (TKI). Tyrosine kinases are proteins that allow cells to communicate with one another and signal each other to rise. Chemical messengers play a role in their function. There are many types of tyrosine kinases, and inhibiting them prevents cancer cells from multiplying.
2	BTK Inhibitor/Ibrutinib	Chronic leukemia (CLL) or small lymphoma (SLL)
3	Anagrelide hydrochloride/Platelet reducing agent	Treatment of patients with thrombocythemia, secondary to myeloproliferative disorders
4	Bexarotene/Retinoid	Cutaneous T-cell lymphoma (CTCL) in patients
5	Chlorambucil /DNA-damaging agent	Chronic lymphocytic leukemia (CLL)
6	Glasdegib/Hedgehog pathway inhibitor	Newly-diagnosed acute myeloid leukemia (AML)
7	Idarubicin/Antitumor antibiotic	Acute myeloid leukemia in adults
8	Ivosidenib/Isocitrate dehydrogenase-1 (IDH1) inhibitor	Myeloid leukemia (AML)
9	Vincristine/Antimitotic	Chemotherapy agent that is used to treat some types of blood cancer
10	Filgrastim/Growth factor	Acute myeloid leukemia (AML)
11	Idelalisib/Phosphoinositide 3-kinase (PI3K) delta inhibitor	Chronic lymphocytic leukemia (CLL)

TABLE 2: LIST OF LIGAND'S AND THEIR ID'S

S. no.	Ligands	ID's
1	Abacavir	11152
2	Blinatumomab	7384
3	Bosutinib	5710
4	Cefiderocol	10776
5	Cefixime	10898
6	Daptomycin	10904
7	Daunorubicin	7063
8	Econazole	2446
9	Eletriptan	40
10	Felodipine	4190
11	Fidaxomicin	10909
12	Gabapentin	5483
13	Gentamicin	2427
14	Lofepramine	7551

Docking: Docking a lock-and-key mechanism where you want to find the correct relative "key" route to activate the "lock". In this case, The protein may be considered the "lock" and the ligand as the "door". Sub-atomic docking is a way to streamline a ligand which links to a particular protein of concern "high-quality-healthy" routes. Since both protein and the ligand are adaptable, the "hand-to-hand" courtship will be stronger than the "lock-and-key" courtship. The ligand and protein share their conformity with the molecular docking relationship to achieve a big "fine-fit", which results in the general restriction and is called a triggered play.

The computational replication of the sub-atomic acknowledgment measure is a specialty of molecular docking study. It means performing a sophisticated version for each protein and ligand, as well as the relative direction between protein and ligand, with the aim of limiting the general framewor's unrestricted electricity.

The molecular docking method is used to model the association between a small molecule and a protein at an atomic level, which enables us to reflect small molecular interaction inside the target protein binding web page and to identify the main biochemical strategies [19].

The Docking Protocol Consists of Two main Phases: Prediction and orientation of the ligand conformation in these websites (usually referred to as poses) and binding evaluation of affinity you must obey certain actions, which are applicable to sampling strategies and scoring systems, if you want to be part of the definition section.

Both biological procedures rely on molecular recognition, so researchers have made genius efforts to identify and predict protein-linking interactions. It is important in drug development to locate a molecule that will undoubtedly bind to a protein, but also a time-consuming, costly process. In silicon techniques molecular libraries for new lead compounds are commonly screened and a collection of protein ligand docking programs may be utilized if protein structure is taken into account.

The aim of the docking technique is to correctly forecast and perform ligand structures in the protein's binding website over time based on the degree of the interaction. The aim of our study was to suggest a progressive consensus approach for predicting both the form and binding affinity of protein-ligand complexes.

RESULT AND DISCUSSION: Docking is a method for predicting the best way for one molecule to interact with another while they're joined to create a stable complex. Also, there are different software's which are used for docking. Thus, here Autodock [20] and also discovery studio software's are used for docking with FLT3 tyrosine kinase Protein [21].

Various Binding energy were identified as the best binding energy was found to be of Abacavir with Flt3 receptor is -7.31 and are listed in **Table 3.**

Result No.1, **Fig. 1:** Software used is Autodock and discovery studio in which Binding energy of Abacavir with FLT3 Receptor is -7.31.

Result No.2, **Fig. 2:** Software used is Autodock and discovery studio in which Binding energy Gabapentin with Flt3 receptor is -4.7.

Result No.3, **Fig. 3:** Software used is Autodock and discovery studio in which Binding

Energy of Gentamicin with Flt3 receptor is -5.46

Result No.4, **Fig. 4:** Software used is Autodock and discovery studio in which Binding energy of Cefixime with Flt3 receptor is -5.34.

Result No.5, **Fig. 5:** Software used is Autodock and discovery studio in which Binding energy of Econazole with Flt3 receptor is -6.74.

TABLE 3: LIGANDS USED AND THEIR BINDING ENERGY

S. no.	Ligands	Ligand ID's	MWT (g/mol)	XLOGP	HBD	HBA	PSA ($Å^{2}$)
1	Abacavir	11152	286.33	0.9	3	6	101.88
2	Blinatumomab	7384	54086.56				
3	Bosutinib	5710	548.5	5.4	1	8	82.88
4	Cefiderocol	10776	752.2	1	6	15	310
5	Cefixime	10898	453.5	-0.7	4	12	184.51
6	Daptomycin	10904	1620.7	-5.1	22	28	702
7	Daunorubicin	7063	527.5	1.8	5	11	186
8	Econazole	2446	381.7	5.3	0	2	27.05
9	Eletriptan	40	382.5	4.1	1	3	53.17
10	Felodipine	4190	383.06	3.9	1	5	64.6
11	Fidaxomicin	10909	1056.42	6.4	7	18	267

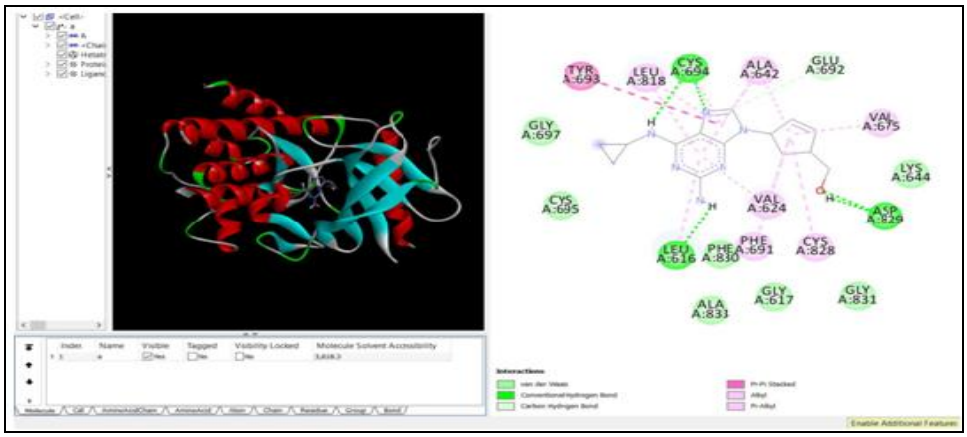

FIG. 1: BINDING ENERGY OF ABACAVIR WITH FLT3 RECEPTOR IS -7.31

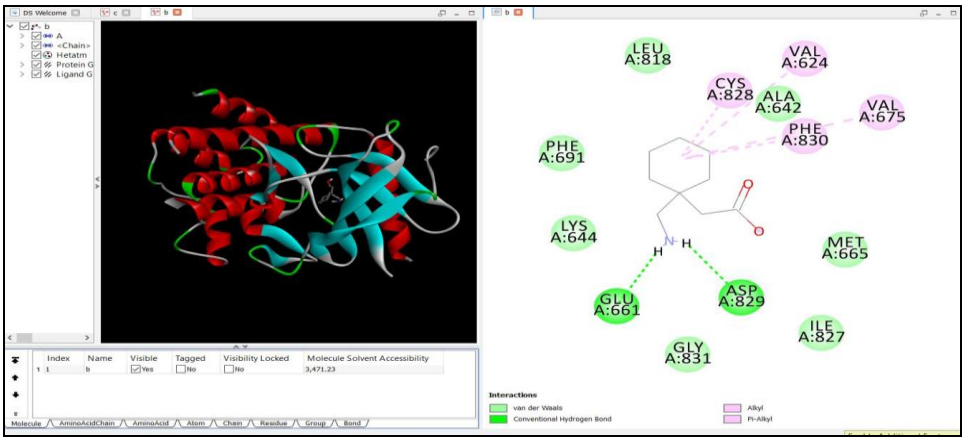

FIG. 2: BINDING ENERGY FOR GABAPENTIN WITH FLT3 RECEPTOR IS -4.7

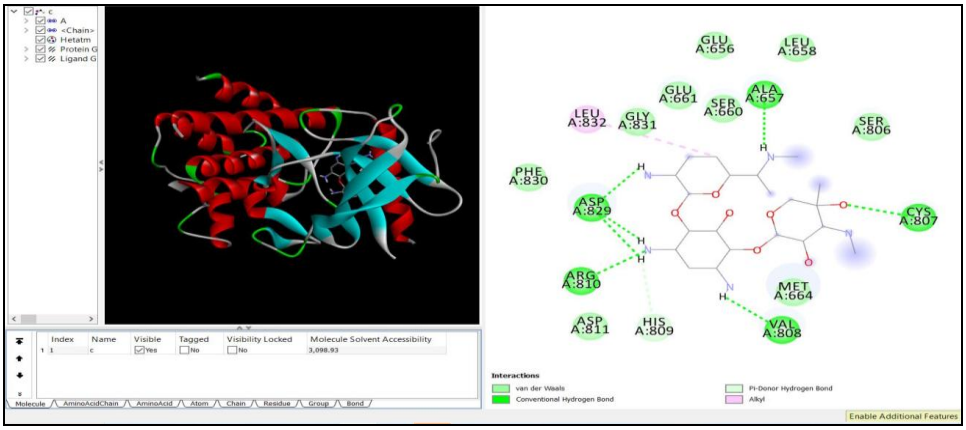

FIG. 3: BINDING ENERGY FOR GENTAMICIN WITH FLT3 RECEPTOR IS -5.46

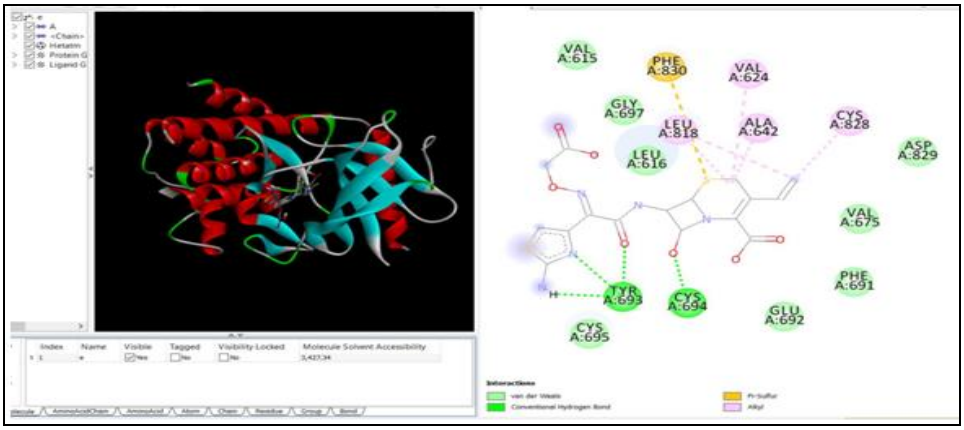

FIG. 4: BINDING ENERGY FOR CEFIXME WITH FLT3 RECEPTOR IS -5.34

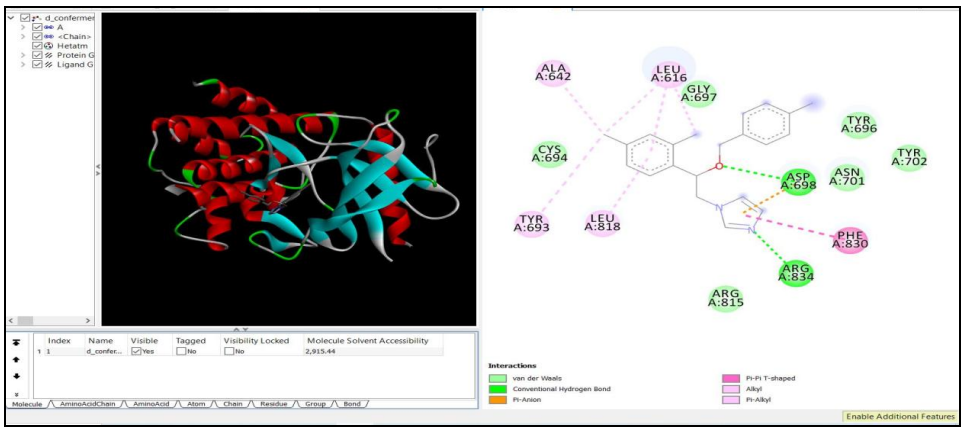

FIG. 5: BINDING ENERGY FOR ECONAZOLE WITH FLT3 RECEPTOR IS -6.74

CONCLUSION: We know that nuclear hormone receptor is FLT3 tyrosine Protein kinase. The eukaryotic gene expression involves the receptors and the steroid hormones to effect cellular proliferation and differentiation in target tissues. Therefore, it is used as a Drug Target. Most pharmaceutical industries use docking software to design new drugs 22 with excellent efficacy and low price. This drug designing method helps in identifying the best inhibitor for any disease and decreases their costs. FLT3 tyrosine-protein kinase was used as a drug target, and inhibitors were identified. Various Binding energy was identified as the best binding energy was found to be of Abacavir with Flt3 receptor is -7.31. The docking work involves the best binding energies using Autodock and discovery studios for drugs as inhibitors and interaction with FLT3 receptors.

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CONFLICTS OF INTEREST: Nil

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