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# IN-SILICO STUDY OF GREEN TEA LEAVES AS AN ANTI-ARTHRITIS TARGETING FOLATE RECEPTOR

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## ABSTRACT

The study involves the molecular docking of the chemical constituents of Green tea leaves, with a specific focus on their potential anti-arthritis activity. The information provides a comprehensive overview of the drug discovery and development process, the molecular docking technique, arthritis types and causes, and the botanical aspects of Green tea leaves, the aim, objective, plan of work, and experimental methods for the in-silico study are detailed, along with the findings and conclusions of the molecular docking study. It aims to contribute to the understanding of the potential anti-arthritis properties of Green tea leaves and the design of effective Molecules of arthritis treatment.

**KEYWORDS:** In Silico Study, Green tea leaves, Anti-arthritis Therapy, Folate receptor4KMZ, Phytoconstituents, Ligands, Receptors, Virtual Screening.

## 1. INRODUCTION

### 1.1 Drug Discovery and Development

Drug discovery has a long history and dates back to the early days of human civilization. In those ancient times, treatments were often discovered by chance or resulted from observation of nature, typically but not exclusively, using ingredients extracted from plants/animals, and not just used for physical remedy but also for spiritual healing.

Modern drug discovery research started to being performed around the early 1900s. Nowadays, the development of a new medicine usually starts when basic research, often performed in academia, identifies a macromolecule (i.e., a molecule with a large molecular

weight like genes/proteins), or a dysfunctional signalling pathway or a molecular mechanism apparently linked to a disease condition (Pre-discovery stage). In general, at this stage, research teams attempt to identify the so-called therapeutic targets (Often a protein) that are linked to the disease state. To be nominated therapeutic target, scientists will also have to find therapeutic agents that modify the function of the perturbed target and restore health or alleviate symptoms. Finding the right target is however extremely challenging. Further, drugs are efficient in humans because of specific actions on the intended therapeutic target but also due to interactions with other, unintended (Often unknown) targets!

The process continues with the search of therapeutic agents followed by a preclinical phase, during which potential drugs are tested in a battery of animal models, to demonstrate safetyand select drug candidates (Novel strategies to avoid animal testing are being developed, see below). Clinical studies in humans can then get started to establish safety and efficacyof the drugs in patients with the highest benefit-to-risk ratio. The studies are then submitted to regulatory agencies, which review the documents and decide about market approval. If the review is positive, the drug can then be released to the market and be administrated to patients.

Once a drug has been approved, investigations continue to monitor putative side effects that could be caused, over time, by the new treatment. This last step is often referred to as pharmacovigilance studies (or real-world evidence), generally dubbed “phase 4” clinical trial. The entire drug discovery and development process involves many disciplines, yearsof efforts and is very expensive. It also implies the generation and use of vast amount of data usually obtained via different types of high-throughput technologies. Many of these experiments and the analysis of the results can be automated via computer-assisted methodsto speed-up some steps of the process, gain knowledge and reduce mistakes.[1]

There are several stages in the drug discovery process that require numerous skills and theuse of various advanced technological platforms (often a combination of computational and experiment, translational, and clinical models see, e.g,[2,3] Despite advances in biotechnology and understanding of biological systems, drug discovery is still a lengthy, costly, difficult, and inefficient process with a high attrition rate of new therapeutic discovery. Drug design is the inventive process of finding new medications based on the knowledge of a biological target. In the most basic sense, drug design involves the design of molecules that are complementary in shape and charge to the molecular target with whichthey interact and bind.

Drug design frequently but not necessarily relies on computer modeling techniques and bioinformatics approaches in the big data era. In addition to small molecules, biopharmaceuticals and especially therapeutic antibodies are an increasingly important class of drugs and computational methods for improving the affinity, selectivity, and stability of these protein-based therapeutics have also gained great advances.[4] Drug development and discovery includes preclinical research on cell-based and animal models and clinical trials on humans, and finally move forward to the step of obtaining regulatory approval in order to market the drug. Modern drug discovery involves the identification of screening hits, medicinal chemistry and optimization of those hits to increase the affinity, selectivity (to reduce the potential of side effects), efficacy/potency, metabolic stability (to increase the half-life), and oral bioavailability. Once a compound that fulfills all of these requirements has been identified, it will begin the process of drug development prior to clinical trials. Drug discovery has a long history and dates back to the early days of human civilization. In those ancient times, treatments were often discovered by chance or resulted from observation of nature, typically but not exclusively, using ingredients extracted from plants/animals, and not just used for physical remedy but also for spiritual healing. Modern

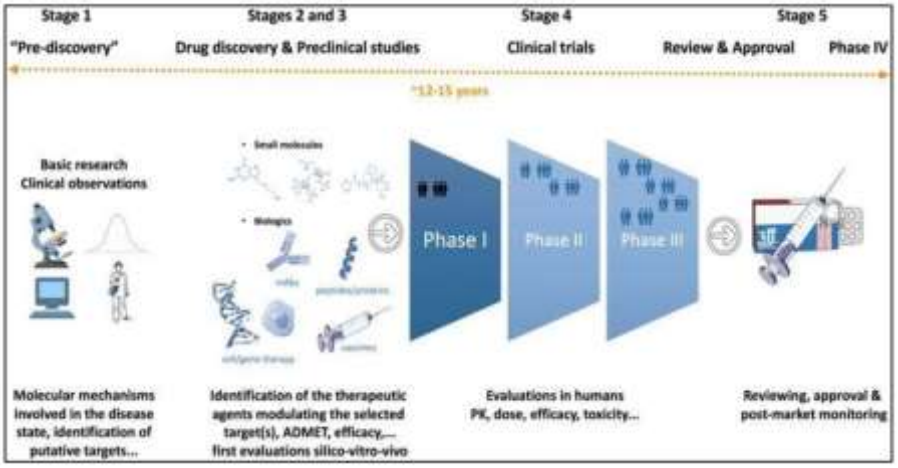



**Figure 1: Drug Discovery and Development.**

### 1.2 Molecular docking

In the meadow of molecular modelling, docking is a technique which predict the prefer direction of one molecule to a second when jump to each other to form a steady compound.[2] Information of the chosen direction in rotate may be worn to expect the strength of involvement or binding affinity linking two molecules with each, for example, score function. The relations between physically appropriate molecules such as proteins, peptides, nucleic acids, carbohydrates, and lipids play a central role in signal transduction. Furthermore, the relative

orientation of the two interact associates may involve the type of signal formed (e.g., agonist vs antagonism). Therefore, docking is helpful for predict both the potency and type ofsignal produced. Molecular docking is one of the majorities generally used technique in structure-based drug design, due to its capability to forecast the binding-conformation of smallmolecule ligands to the suitable target binding site. Characterization of the binding performance plays a significant role in rational plan of drugs as well as to explain fundamentalbiochemical process.[3] The aim of molecular docking is to accomplish an optimized conformation for both the protein and ligand and fundamental direction between protein and ligand so that the free energyof the generally method is minimized.[4] Molecular recognitionplays a key role in promote elementary bimolecular proceedings such as enzyme substrate, drug-protein and drugnucleic acid interactions.[5] Detailed appreciative of the universal principles that administrate the.

**Stages of drug Discovery and Development**

- Target identification
- Target validation
- Lead identification
- Lead optimization
- Product characterization
- Formulation and Development
- Preclinical research
- Investigational New Drug Application
- Clinical trial
- New Drug Application
- FDA Review
- Approval

**Molecular docking**

Molecular docking, a computational method, has become indispensable in modern drug discovery and structural biology. It enables the prediction and analysis of the binding affinity and orientation of small molecules with target proteins.[8,9] This article servesas a primer on molecular docking, elucidating its fundamental concepts and exploring various types of docking techniques employed in pharmaceutical research.

**Understanding molecular docking**

At its core, molecular docking involves simulating the binding process between a ligand and a receptor to predict their complex structure and binding affinity. The process relies on algorithms that evaluate intermolecular interactions such as van der Waals forces, hydrogen bonding, and electrostatic interactions.[10] The main objectiveof molecular docking is to attain ligand-receptor complex with optimized conformationand with the intention of possessing less binding free energy. The net predicted binding free energy (ΔGbind) is revealed in terms of various parameters, hydrogen bond (ΔGhbond), electrostatic (ΔGelec), torsional free energy (ΔGtor), dispersion and repulsion (ΔGvdw), desolvation (ΔGdesolv), total internal energy (ΔGtotal) and unbound system's energy (ΔGunb). Therefore, good understanding of the general ethics that govern predicted binding free energy (ΔGbind) provides additional clues about the nature of various kinds of interactions leading to the molecular docking.

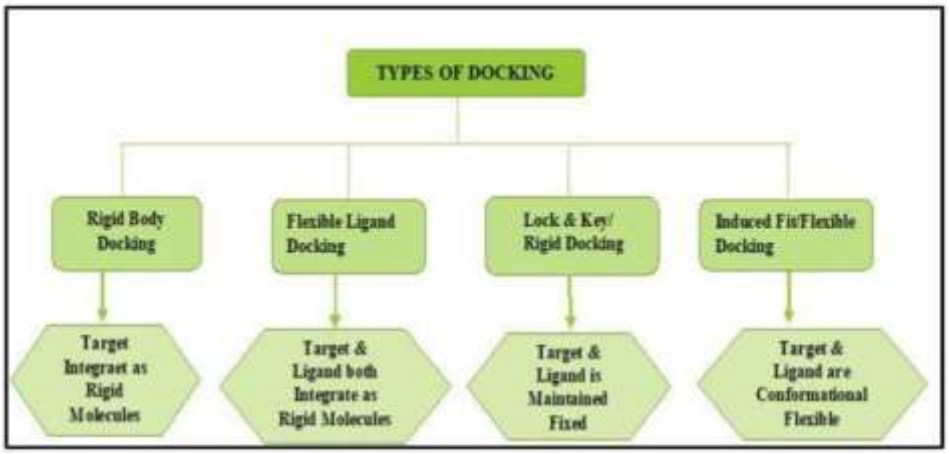



**Figure 2: Types of molecular docking.**

Nature of the connections (Van der Waals, Hydrogen bonding, Electrostatic) involving the


**Figure 3: Drug development process.**

Ligands and their protein or nucleic acid targets may afford a framework for designing the most wanted potency and specificity of potential drug leads for a given therapeutic target.[6] Practical application of this information requires structural data for the goal of significance and a progression for evaluating candidate ligand.[7] A variety of computational docking methods are accessible.[8]

**Types of docking**

**Types of molecular docking techniques**

1. **Rigid docking**

- In rigid docking, both ligand and receptor structures are held fixed without considering conformational changes.
- This method is efficient for exploring initial binding interactions but may overlook the flexibility of molecules.

2. **Flexible docking**

- Flexible docking allows for conformational changes in both ligand and receptor during the binding process.
- Molecular dynamics simulations or ensemble docking methods are often employed to account for flexibility, enhancing the accuracy of predictions.

3. **Ligand-Based Docking**

- Ligand-based docking relies on the structural information of ligands to predict their binding poses and affinity.
- Techniques such as pharmacophore modeling and shape-based docking are used to identify molecules with similar features to known ligands.

4. **Structure-Based docking**

- Structure-based docking utilizes the three-dimensional structure of the target protein to predict ligand binding.
- Grid-based methods, such as AutoDock, and scoring functions are commonly employed in structure-based docking to predict energetically favorable binding poses.

**1.2.1. Applications of molecular docking**

Molecular docking serves as an invaluable tool across various facets of drug discovery and development:

- Lead optimization
- Hit Identifications
- Drug-DNA Interactions Studies
- Drug Repurposing
- Virtual Screening
- Target discovery

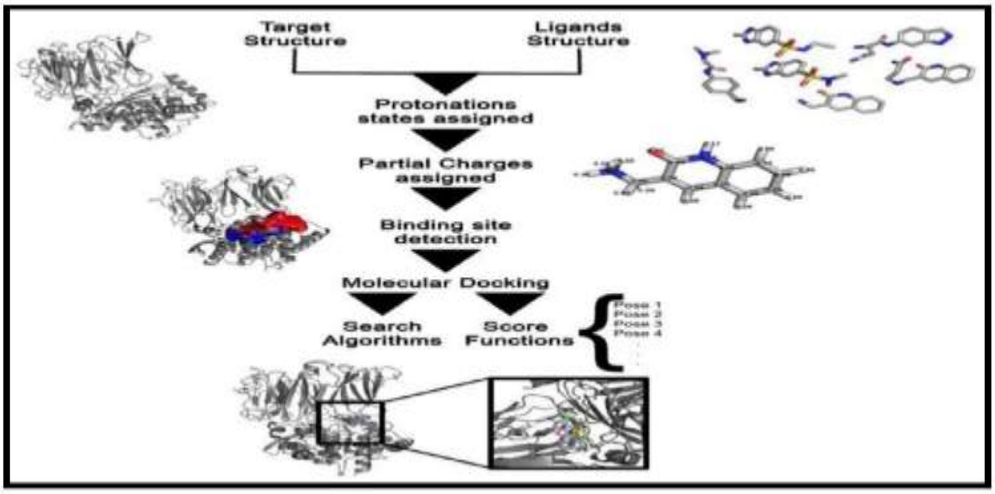



**Figure 4: General workflow of molecular docking calculation.**

**Disease:** Arthritis

Arthritis refers to more than 100Trusted Source rheumatic diseases and conditions that affect joints. These conditions tend to involve pain, aching, stiffness, and swelling in and around one or more joints.

The word "arthritis" means "joint inflammation." However, inflammation may also affect the tendons and ligaments surrounding the joint. The symptoms can develop gradually or suddenly and may impair a person's ability to perform everyday tasks.

**Types of arthritis**

There are more than 100 types of arthritis. Generally, arthritis can be split into the following categories:

**Inflammatory arthritis**

Inflammation is a normal part of the body's healing process. It tends Trusted Source to occur as a defense against viruses and bacteria or as a response to injuries such as burns. However, with inflammatory arthritis, inflammation occurs in people for no apparent reason.

Inflammatory arthritis is characterized by damaging inflammation that does not occur as a normal reaction to injury or infection. This type of inflammation is unhelpful and instead causes damage to the affected joints, resulting in pain, stiffness, and swelling.

Inflammatory arthritis can affect several joints, and the inflammation can damage the surface of the joints and also the underlying bone.

**Examples of inflammatory arthritis include**

- RA
- Reactive arthritis
- Ankylosing Spondylitis
- Psoriatic Arthritis

**Degenerative or mechanical arthritis**

Degenerative or mechanical arthritis refers to a group of conditions that mainly involve damage to the cartilage that covers the ends of the bones.

The main job of the smooth, slippery cartilage is to help the joints glide and move smoothly. This type of arthritis causes the cartilage to become thinner and rougher.

To compensate for the loss of cartilage and changes in joint function, the body begins to remodel the bone in an attempt to restore stability. This can cause undesirable bony growthsto develop, called osteophytes. The joint can become misshapen. This condition is commonly Trusted Source called osteoarthritis.

Osteoarthritis can also result from previous damage to the joint such as a fracture or previous inflammation in the joint.

**Connective tissue disease (CTD)**

Connective tissues support, bind together, or separate other body tissues and organs. They include tendons, ligaments, and cartilage.

CTD involves joint pain and inflammation. The inflammation may also occurTrusted Source in other tissues, including the skin, muscles, lungs, and kidneys. This can result in various symptoms besides painful joints, and it may require consultation with a number of different specialists.

**Examples of CTD include**

- SLE, or lupus
- scleroderma, or systemic sclerosis
- Dermatomyositis
- Sjogren's

**Infectious arthritis**

A bacterium, virus, or fungus that enters a joint can sometimes cause inflammation.

Organisms that can infect joints include:

- Salmonella and shigella, which spread through food poisoning or contamination
- Chlamydia and gonorrhea, which are sexually transmitted diseases (STDs)
- Hepatitis C, which is a blood-to-blood infection that may be spread through sharedneedles or transfusions

A doctor can treat a joint infection with antibiotics or other antimicrobial medication. However, the arthritis can sometimes become chronic, and joint damage may be irreversibleif the infection has persisted for some time.

**Metabolic arthritis**

Uric acid is a chemical created when the body breaks down substances called purines.Purines are found in human cells and several foods.

Most uric acid dissolves in blood and travels to the kidneys. From there, it passes out of the body in urine. Some people have high uric acid levels because they either naturally produce more than they need or their body cannot clear the uric acid quickly enough.

Uric acid builds up and accumulates in some people and forms needle-like crystals in thejoint, resulting in sudden spikes of extreme joint pain or a gout attack.

Gout can either come and go in episodes or become chronic if uric acid levels are notreduced.

It commonly affects a single joint or a small number of joints, such as the big toe and hands.It usually affects the extremities. One theory is that uric acid crystals form in cooler joints, away from the main warmth of the body.

Some of the more common types of arthritis are discussed below.

**Childhood arthritis**

This can refer to a number of types of arthritis. Juvenile idiopathic arthritis (JIA), also known as juvenile rheumatoid arthritis (JRA), is the most common Trusted Source type.

Arthritis in childhood can cause permanent damage to joints, and there is no cure. However, remission is possible, during which time the disease remains inactive.

**Symptoms of arthritis**

The symptoms of arthritis that appear and how they appear vary widely, depending on the type.

They can develop gradually or suddenly. As arthritis is most often a chronic disease,symptoms may come and go, or persist over time.

However, anyone who experiences any of the following four key warning signs should see a doctor.

1. **Pain:** Pain from arthritis can be constant, or it may come and go. It may affect onlyone part or be felt in many parts of the body.
2. **Swelling:** In some types of arthritis, the skin over the affected joint becomes red and swollen and feels warm to the touch.
3. **Stiffness:** Stiffness is a typical symptom. With some types, this is most likely uponwaking up in the morning, after sitting at a desk, or after sitting in a car for a long time. With other types, stiffness may occur after exercise, or it may be persistent.
4. **Difficulty moving a joint:** If moving a joint or getting up from a chair is hard orpainful, this could indicate arthritis or another joint problem.

In addition to these general signs, certain types of arthritis may cause their own unique symptoms. For example, Juvenile RA can cause eye problems, including uveitis, iridocyclitis, or iritis.

Septic arthritis often causes fever and intense joint pain. It can become an emergen.

**Causes of arthritis**

There is no single cause of all types of arthritis. The cause or causes vary according to thetype or form of arthritis.

**Possible causes may include**

- An injury, which can lead to degenerative arthritis
- An abnormal metabolism, which can cause gout and calcium pyrophosphate deposition disease (CPPD)
- A genetic inheritance, which can lead to developing osteoarthritis
- An infection such as Lyme disease, which can trigger arthritis symptoms
- An immune system dysfunction, such as the type that causes RA and lupus

Most types of arthritis are linked to a combination of factors. However, some have no obvious cause and appear to be unpredictable in their emergence.

**Treatment of arthritis**

Treatment for arthritis aims to control pain, minimize joint damage, and improve or maintain function and quality of life. A range of medications and lifestyle strategies can help achieve this and protect joints from further damage.

The exact treatment depends on the type of arthritis a person develops. It may involveTrusted Source:

**Medication**

Medications will depend on the type of arthritis. Commonly used drugs include:

- **Analgesics:** These reduce pain. However, they have no effect on inflammation. Examples include acetaminophen (Tylenol) and tramadol (Ultram).
- **Nonsteroidal anti-inflammatory drugs (NSAIDs):** These reduce both pain and inflammation. NSAIDs include available to purchase over-the-counter or online, including ibuprofen (Advil, Motrin IB) and naproxen sodium (Aleve). Some NSAIDs are available as creams, gels, or patches, which can be applied to specific joints.
- **Counterirritants:** Some creams and ointments contain menthol or capsaicin, the ingredient that makes hot peppers spicy. Rubbing these on the skin over a painful jointcan modulate pain signals from the joint and lessen pain.
- **Disease-modifying antirheumatic drugs (DMARDs):** These are used to treat RA. DMARDs slow or stop the immune system from attacking the joints. Examples include methotrexate (Trexall) and hydroxychloroquine (Plaquenil).
- **Biologics:** These are genetically engineered drugs that target various protein molecules involved in the immune response. Examples include etanercept (Enbrel) and infliximab (Remicade).

- **Corticosteroids:** prednisone and cortisone reduce inflammation and suppress theimmune system.

**Plant**

**Green tea leaves**

Biological Name - *Camellia sinensis*

Family- Theaceae family

Genus - Camellia Sinensis

The health benefits of green tea for a wide variety of ailments, including different types of cancer, heart disease, and liver disease, were reported. Many of these beneficial effects of green tea are related to its catechin, particularly (-)-epigallocatechin-3-gallate, content. There is evidence from *in vitro* and animal studies on the underlying mechanisms of green tea catechins and their biological actions. There are also human studies on using green tea catechins to treat metabolic syndrome, such as obesity, type II diabetes, and cardiovascular risk factors.

Long-term consumption of tea catechins could be beneficial against high-fat diet-induced obesity and type II diabetes and could reduce the risk of coronary disease. Further research that conforms to international standards should be performed to monitor the pharmacological and clinical effects of green tea and to elucidate its mechanisms of action.

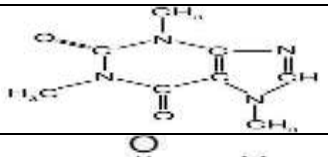
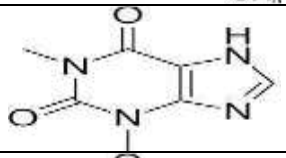
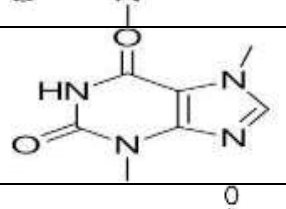
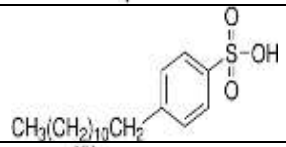
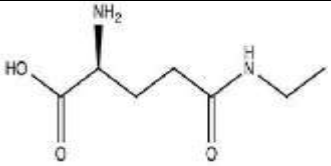
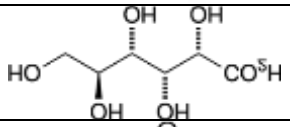
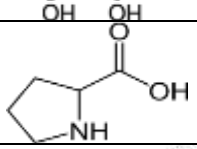
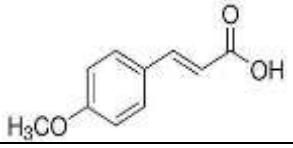
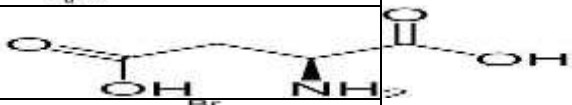
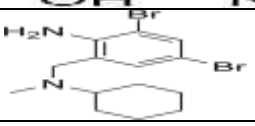
Biological source - Green tea comes from the plant Camellia sinensis. Black tea, green tea,and oolong tea are all made from the same plant but are prepared using different processing methods. Green tea extract contains polyphenols. These include the most active type, epigallocatechin gallate.

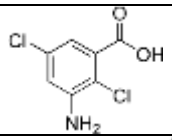
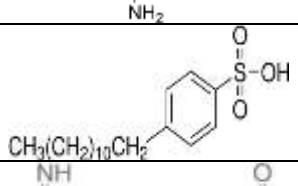
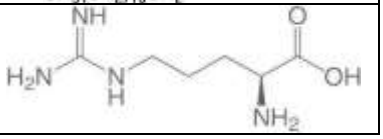
Chemical constituents - Green tea contains polyphenols, which include flavanols, flavandiols,

flavonoids, and phenolic acids; these compounds may account for up to 30% of the dry weight.

Uses -As a drink or supplement, green tea is sometimes used for high cholesterol, high blood pressure, to prevent heart disease, and to prevent ovarian cancer. It is also used for many other conditions, but there is no good scientific evidence to support most of these uses.

**Table 1: Chemical constituents.**

| Sr. No. | Chemical constituents | Structures |
|---|---|---|
| 1. | Caffine |  |
| 2. | Theophylline |  |
| 3. | Theobromine |  |
| 4. | Linoleic |  |
| 5. | Theanine |  |
| 6. | Glutamic Acid |  |
| 7. | Glutamic Acid |  |
| 8. | Serine |  |
| 9. | Aspartic Acid |  |
| 10 | Valine |  |

| | | |
|---|---|---|
| 11 | Threonine |  |
| 12 | Arginine |  |
| 13 | Luteolin |  |

## 2. AIM AND OBJECTIVE

### Aim

To perform virtual screening of biologically active ligands which is Anti-Arthritis drugs on f 4KMZ. Folate receptor.

### Objective

- To design the Chemical Constituents of Green tea leaves.
- To study the molecular docking of the Chemical Constituents of Green tea leaves.
- To Study the Physicochemical properties.
- To Evaluate the ADME study.

## 3. Plan of work

- Downloading and installing all the required software Program
- Preparation of the Ligands
- Preparation of Receptor
- Virtual Screening
- SwissADME (Evaluate Physicochemical Properties)

## 4. Experimental work

### 4.1 Downloading and Installing all the required software program

a) Chemsketch

b) Avogadro

c) PyRx

d) Discovery studio

### a) Chemsketch

This open-source software is a chemical molecule or molecular modelling program used to

create, draw and modify images of chemical structures or compounds and there is software that allows molecule and molecular models displayed in two and three dimensions, to understand the structure of chemical bonds and nature of the functional groups. This tool enables us to draw chemical molecules and save them directly in several formats like. mol, .jpg, .png and many more formats. We can also generate the international union of pure and applied chemistry(IUPAC) of the chemical structures. ChemSketch is a molecular modelling program used to create and modify images of chemical structures. Also, there is a software that allows moleculesand molecular models displayed in two and three dimensions, to understand the structure of chemical bonds and the nature of the functional groups. This software also helps us for generation of simplified molecular input line entry system (SMILES) of the desired chemical structure.[16]

**b) Avogadro software**

Avogadro software was used to convert the. mol file to. pdb format. This is again opensource software that helps optimize the chemical structure. This also helps in minimizing the energy which is very important protocol for in silico studies. The software also allows generation of structure through SMILES or by drawing tool. These chemical structures were saved in the format of .pdb format which is required for docking purpose.[16]

**c) PyRx software**

PyRx software was used for virtual screening of library of derivatives. The pyrx software is a open software for virtual screening. The approach includes blasting of several ligand moleculesto a target and segregate the best fit molecules from the library. The tool includes a 4step protocol and can screen a big library of molecules simultaneously on a defined site of target/receptor. The results can easily be exported in Microsoft excel format as .csv file.[16]

**d) Biovia discovery studio**

BIOVIA Discovery Studio brings together over 30 years of peer-reviewed research and worldclass in silico techniques such as molecular mechanics, free energy calculations, biotherapeutics developability and more into a common environment. It provides researchers with a complete toolset to explore the nuances of protein chemistry and catalyse discovery of small and large molecule therapeutics from Target ID to Lead Optimization.[16]

**With discovery studio you can**

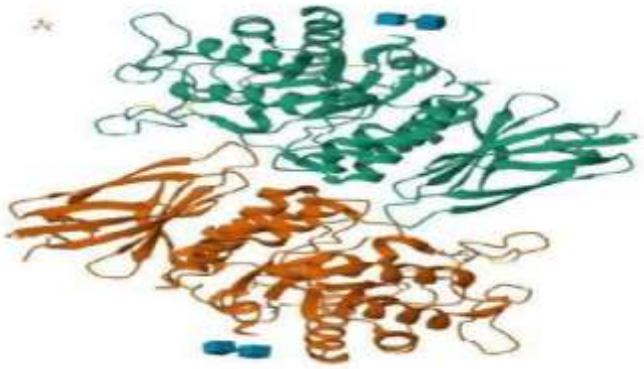
- Investigate and test hypotheses in silico prior to costly experimental implementation, thus reducing the time and expense involved in bringing products to market
- Drive scientific exploration from target identification to lead optimization with a wealth of trusted life science modelling and simulation tools
- Leverage BIOVIA Pipeline Pilot to automate processes, create and deploy custom workflows, and integrate data types, databases, and third-party or in-house tools.

### 4.2 Preparation of ligands

Library of active phytochemicals of Green Tea Leaves plant species which is responsible for anti-arthritis activity were retrieved from literature. PubChem compound database (https://pubchem.ncbi.nlm.nih.gov) was used for the retrieval of structures in PDB (Protein data bank) format. Preparation of ligand file used the software's and online library from the PubChem for their specification Smiles notation were copied from PubChem database and thenstructure was generated from this smile notation in ChemSketch afterwards this smile notationwas used to retrieve ligands to 3D PDB format with the help of Avogadro software.

### 4.3 Preperation of receptor

RCSB (Research Collaboratory for Structural Bioinformatics) Protein Data Bank was usedto retrieve the three-dimensional structure of receptor PDB ID: 1dlr download the structure in .pdb format from the online database and was rectified using auto dock software which is already present in the PyRx software. Preparation of receptor was done with the help of Discovery studio. The pdb format is opened in the discovery studio and then press Ctrl + H andthen remove the pre-associated ligand present in the receptor alsoheteroatoms and water molecules present in structure were cleaned and the active sites were identified and then savedin the working folder as pdb file.



## 5. RESULT AND DISCUSSION

The docking of the receptor 4KMZ with chemical constituents of Green tea leaves has been done. The table shows the binding affinity and inhibition constant of 15 compounds includingstandard. In silico studies revealed that all the chemical constituents show good binding affinitytoward the target.

**Table No. 2: Ligands with their binding affinity.**

| | Ligands | Binding affinity |
|---|---|---|
| 1. | Caffine | -5.8 |
| 2. | Theophylline | -8.8 |
| 3. | Theobromine | -6.6 |
| 4. | Linoleic | -9 |
| 5. | Theanine | -8 |
| 6. | Glutamic Acid | -5.5 |
| 7. | Tryptophan | -7.4 |
| 8. | Gycine | -6.4 |
| 9. | Serine | -8.2 |
| 10. | Aspartic Acid | -9.9 |
| 11. | Tyrosine | -8.3 |
| 12. | Valine | -10.4 |
| 13. | Threonine | -7.3 |
| 14. | Arginine | -7.8 |

### 5.1. Interaction of ligands with amino acid residue of dihydro folate receptor with

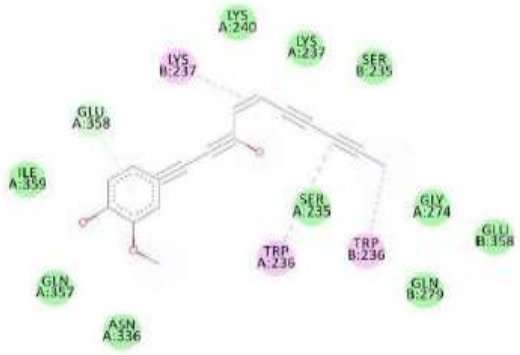



**Figure No. 1: Methotrexate with Receptor 4KMZ.**

Above figure shows the amino acid interaction of standard Methotrexate with 1dlr gives Binding affinity score -9.9

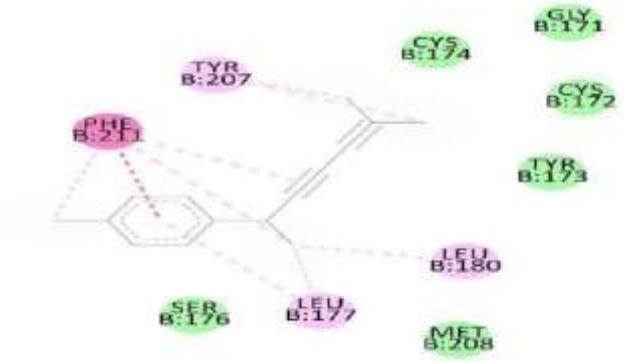



**Figure No. 2: Ligand (R1) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of ellagic acid (R1) with 1dlr gives Binding affinity score -8.3

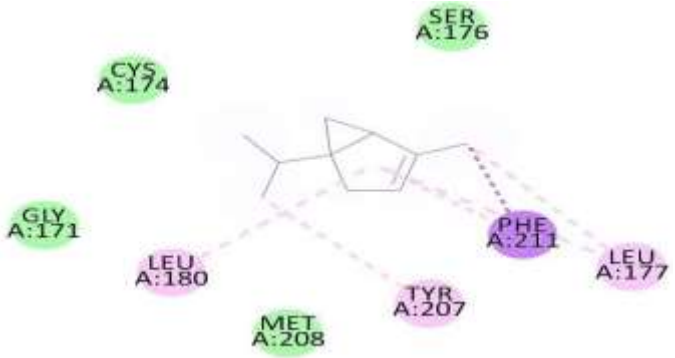



**Figure No. 3: Ligand (R2) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of 1-Tricosene (R3) with 1dlr gives Binding affinity score -7.3

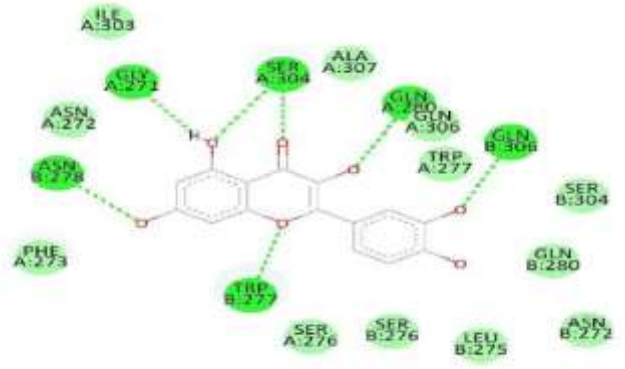



**Figure No. 4: Ligand (R3) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Galic acid (R2) with 1dlr gives Binding affinity score -10.4

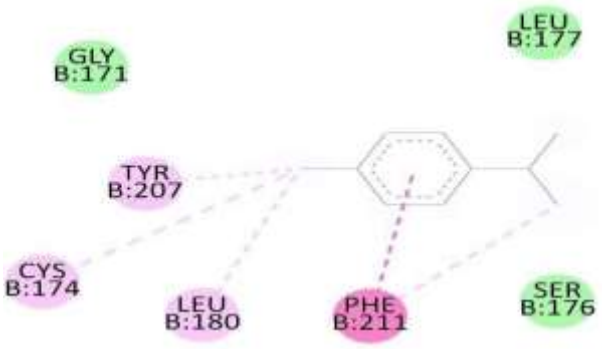



**Figure No. 5: Ligand (R4) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Octadec-9-ene (R4) with 1dlr gives Binding affinity score -7.8

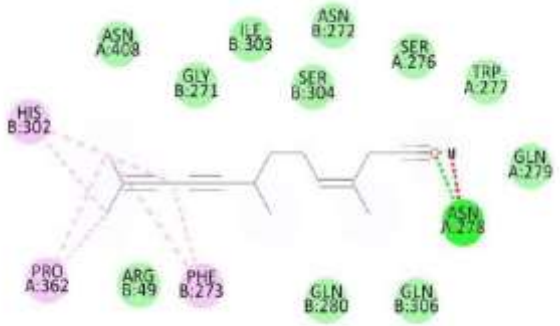



**Figure No. 6: Ligand (R5) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Ethyl Gallate (R5) with 1dlr gives Binding affinity score -6.3

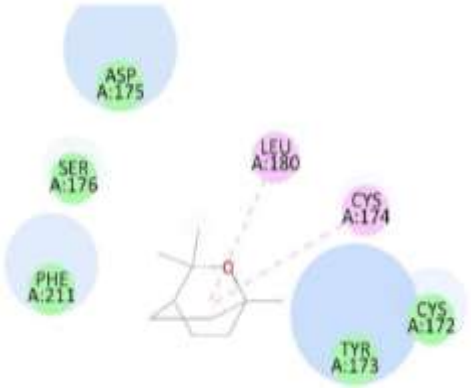



**Figure No7: Ligand (R6) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Gluconic acid (R6) with 1dlr gives Binding affinity score -5.5

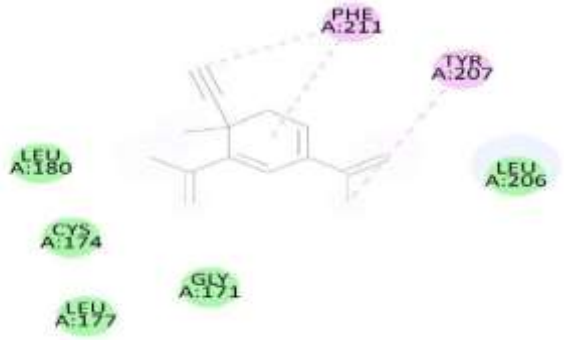



**Figure No. 8: Ligand (R7) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Proline (R7) with 1dlr gives Binding affinity score -4.6

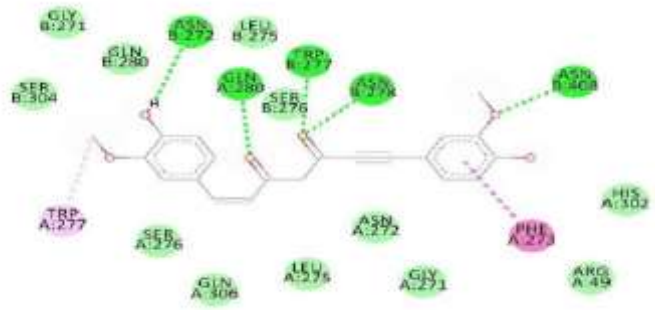



**Figure No. 9: Ligand (R8) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of 4-Methoxycinnamic acid (R8) with 1dlr gives Binding affinity score -6.7

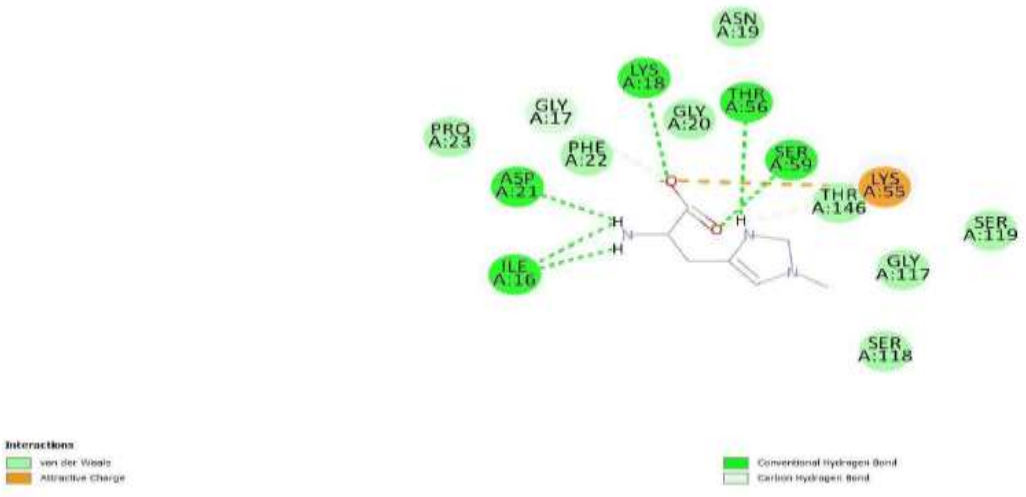



**Figure No. 10: Ligand (R9) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of 1-Methyl Histidine (R9) with 1dlr gives

Binding affinity score -5.8

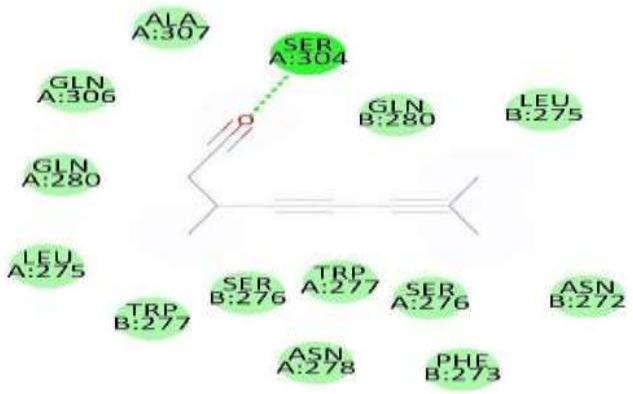



**Figure No. 11: Ligand (R10) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Luteolin (R10) with 1dlr gives Binding affinity score -8.8

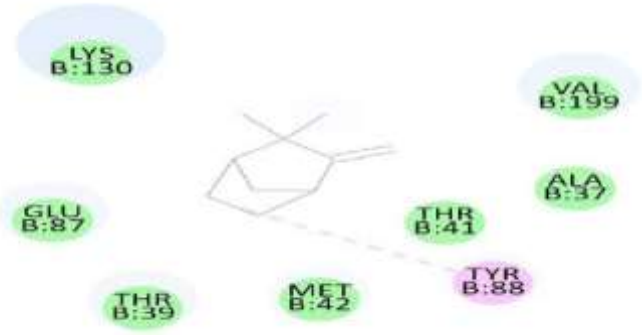



**Figure No. 12: Ligand (R11) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of Chloramben (R11) with 1dlr gives Binding affinity score -6.6

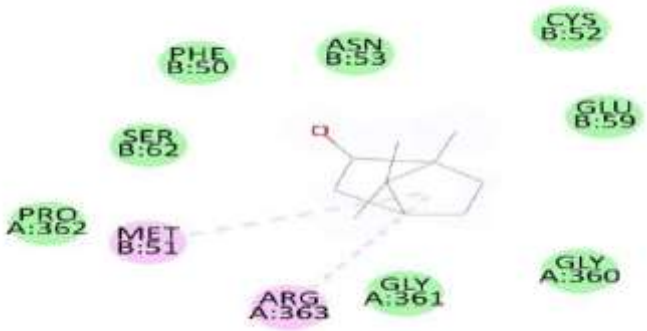



**Figure No. 13: Ligand (R12) with Receptor 4KMZ.**

Above figure shows the amino acid interaction of 4-Dodecylbenzenesulfonic (R12) acid with 1dlr gives Binding affinity score -9

## 6. CONCLUSION

The In-silico study showed Phytoconstituents of the Anti-arthritis having potent Anti-arthritis activity. The study can be extended further in designing effective molecules by the help of Molecular Docking studies. These studies can be helpful to design molecule with better specificity at receptor level and be safe. The compound Arginine shows best affinity towards 4KMZ anti-arthritis receptor. From this Docking results identified the best molecule interact with receptor these selected one molecule used for the anti-arthritis activity Methotrexate standard interactions of amino acid. LYS A 54, LYS A 55, THR A 56, SER A 118, THR A 146,PHE A 22, TYR A 121, ILE A 7 this amino acid found and anti-cancer activity done with withthe PDB ID 1dlr. Figure No. shows the amino acid interaction of Galic acid - 1dlr gives the Binding score -10.4. PRO A 26, PHE A 31, PRO A 61, ILE A 60, VAL A 115, ILE A 7, PHE A34.

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