# *"Screening of phytoconstituents from Acanthus ilicifolious L. for antidepressant activity through in silico molecular docking and ADMET approach"*

[This dissertation is being reported to the Department of Pharmacy at Daffodil International University to satisfy the prerequisites for the Bachelor of Pharmacy Degree partially]

## Submitted To

Department of Pharmacy
Faculty of Health and Life Sciences
Daffodil International University

## Submitted by

ID: 201-29-390
Batch: 23th
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**Date of submission**

# APPROVAL

This project **"Screening of phytoconstituents from *Acanthus ilicifolious L.* for antidepressant activity through in silico molecular docking and ADMET approach"** submitted to the Department of Pharmacy, **Faculty of Health and Life Sciences**, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy and approved as to its style and content.

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# DECLARATION

I, **Sabiha Sultana**, certify that I have completed this assignment under the guidance of **Subrato Kumar Barman**, a lecturer in the Department of Pharmacy at Daffodil International University. I acknowledge that this project has not been previously submitted for evaluation for a bachelor's degree or any other form of recognition.

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# ACKNOWLEDGEMENT

Before anything else, I expressed gratitude to the Almighty for enabling me to complete this endeavor within the designated timeframe. I would like to express my heartfelt appreciation to all those who assisted me in completing this project and contributed to its remarkable success.

A project is not limited to ideas, assessments, and individual effort alone. It needs the assistance and counsel of numerous people to succeed and yield the intended outcome. I consider myself quite fortunate to have obtained this throughout the whole project completion process.

I owe a debt of appreciation and respect to **Professor Dr. Muniruddin Ahmed**, the head of DIU's pharmacy department, for letting me work on this project and for all of his guidance and assistance, which helped me complete the thesis accurately.

I owe a debt of gratitude to **Subrato Kumar Barman**, a lecturer in the pharmacy department, who guided and directed me throughout my project. He gave me all the knowledge I needed to finish the project and establish a working system, and he guided me through the entire process. I appreciate the pharmacy department's teaching staff for their unceasing encouragement, support, and guidance, which helped us finish our project work effectively.

# DEDICATION

# To

# ALMIGHTY ALLAH, MY FAMILY AND

# SUPERVISOR

# ABSTRACT

Studying and developing new medications takes a lot of time, money, and labor. It's also a risky process. It is necessary to follow a methodical approach to find powerful new medications. Because computational methods may integrate physical and molecular processes, they are becoming more and more common in the drug development process. This could lead to lower costs and higher success rates.

The application of medicinal plants for the treatment of Depression is widespread, as herbal medications are generally considered to be devoid of hazardous side effects. Furthermore, the constraints of anti-depressant medications necessitate the search for novel pharmaceuticals to address the therapy of Depression. Consequently, there is ongoing research to find more efficient and safer herbal anti-depressant compounds, as well as to produce novel anti-depressant medications that have better clinical characteristics.

The present effort intends to find and assess potential biological targets, such as proteins or enzymes, that are involved in focused investigations. This will be achieved through the use of molecular docking, a computer-based method. The curated database IMPPAT: Indian Medicinal Plants, Photochemistry and Therapeutics was employed to extract a range of phytochemicals from *Acanthus ilicifolious L.* The phytochemicals are assessed using molecular docking with the protein Human Monoamine Oxidase A (2Z5Y). Several phytochemicals have demonstrated potential binding affinities with specific target proteins.

The objective is to analyze the pharmacokinetic and pharmacodynamic aspects of these compounds as potential therapeutic agents using ADMET prediction and in silico docking investigations of individual phytoconstituents. Molecular docking was also employed to validate these findings

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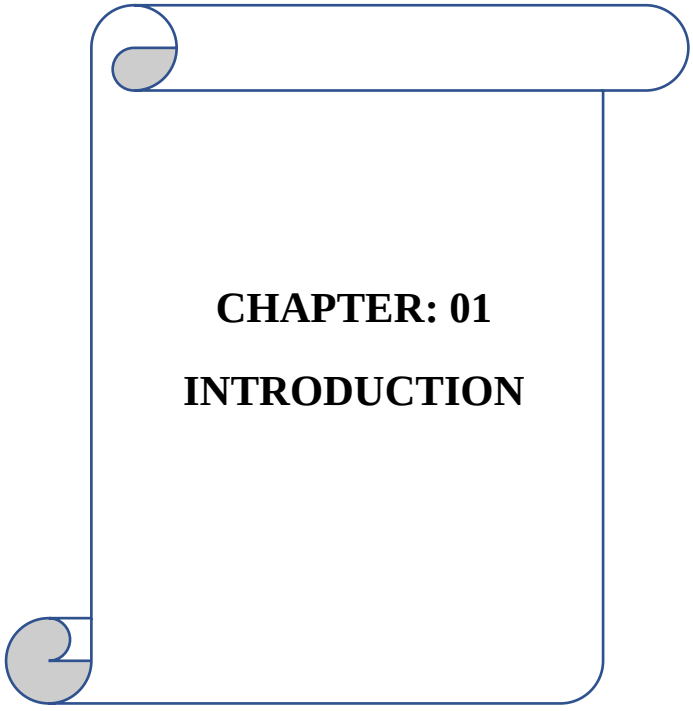


# CHAPTER: 01

# INTRODUCTION

# Chapter One: Introduction

## 1.1: Depression

Depression is a psychiatric condition characterized by a chronic state of melancholy and lack of interest. The characteristics of all depressive disorders include feelings of melancholy, emptiness, or irritability, along with physical and mental changes. Depression can manifest with various psychological and physical symptoms, such as diminished interest or enjoyment in hobbies and activities, alterations in eating and body weight, restlessness in movements, Reduced energy level or tiredness, Insomnia or hypersomnia, Overwhelming sense of guilt or emotions of worthlessness, Impaired ability to focus or make decisions, Contemplation of mortality or self-harm, or instances of attempting suicide, etc. (Chand & Arif., July 17, 2023.).

### 1.1.1: Etiology of depression

Depression is commonly attributed to a chemical imbalance, although such an analogy fails to fully convey the intricate nature of the illness. Studies indicate that depression does not arise solely from an excess or deficiency of specific neurotransmitters in the brain. Instead, depression can be attributed to various factors such as impaired mood regulation in the brain, hereditary susceptibility, and challenging life circumstances. It is widely thought that multiple factors combine to trigger depression.

Indeed, chemicals play an active part in this process, but it is not a case of a single molecule being missing while another is sufficient. Instead, many chemicals are involved, functioning both internally and externally within nerve cells. The dynamic system responsible for your emotions, perceptions, and life experiences consists of millions, or possibly billions, of chemical interactions (Onset of depression more complex than a brain chemical imbalance https://www.health.harvard.edu/mind-and-mood/what-causes-depression, January 10, 2022).

### 1.1.2: Global Status of Depression

The World Health Organization (WHO) reports that there are more than 280 million people worldwide who experience depression. Depression affects persons of all age groups. There are 1.9 million children aged 3 to 17 who have received a diagnosis of depression.

The age cohort exhibiting the highest incidence of depression is persons between the ages of 18 and 29, with a prevalence rate of 21%. Next, for persons between the ages of 45 and 64, as well as those who are older, the prevalence rate among those aged 30 to 44 was slightly lower at 16.8%. The disparity in depression diagnoses between genders can be ascribed to both

societal and biological factors, which contribute to the elevated prevalence of depression among women. The incidence of depression, as well as anxiety, has experienced a substantial rise among young adults. The World Health Organization (WHO) has highlighted social isolation, difficulties in work and family visits, and a feeling of detachment from the community as factors that contribute to the increase in depression and anxiety during the COVID-19 pandemic. (Sabrina Romanoff, 2023)

### 1.1.3: Current Status of Depression in Bangladesh

On a global scale, prevalent mental health illnesses can be broadly categorized into two main groups - anxiety disorders and depressive disorders. Approximately 4.4% of the global population experience depressive disorders, whereas 3.6% suffer from anxiety disorders. In the Western Pacific Region, the depression rate is 3.6%, whereas in the African Region, it is 5.4%. Globally, it is estimated that more than 300 million individuals experience depression, which is equivalent to around 4.4% of the worldwide population.

According to the World Health Organization (WHO), depression is expected to become the primary cause of illness burden by 2030. The frequency of mental health issues among the adult population in Bangladesh showed a substantial drop from 31.4% in 1974 to 16.1% in 2005, however, it remained dangerously high in 2005. The inaugural nationwide mental health study conducted from 2003 to 2005 discovered that 16.1% of the adult populace exhibited symptoms of a mental condition, with a greater occurrence among women (19%) compared to men (12.9%). In their systematic analysis, Hossain et al demonstrate that the prevalence of mental disorders, such as depression, among children in Bangladesh ranged from 13.40% to 22.9% between 1998 and 2004. The array contains the numbers 3 and 4. The prevalence of depressive disorders is estimated to be 4.6%. Regrettably, the provision of mental health treatment is severely lacking as a result of a scarcity of public mental health facilities, a shortage of highly skilled specialists, inadequate allocation of financial resources, and the presence of stigma (Anwar, 2018 )

## 1.2: Available Antidepressants

Selective serotonin reuptake inhibitors (SSRIs) have come to be known as the preferred class of medications for treating depression. These drugs are thought to function by increasing the level of serotonin, a hormone that plays a role in managing one's mood in the brain. Although they are useful in treating depression, these medications usually require approximately 2 weeks to begin showing results and 4 to 8 weeks to achieve their maximum therapeutic effects.

MAOIs effect by decreasing the activity of monoamine oxidase (MAO), a protein. The function of MAO is to metabolize serotonin, norepinephrine, and dopamine. MAOIs increase the amounts of these chemical messengers in the brain by blocking this protein.

Most individuals with depression are frequently cautioned against using MAOIs due to the potential for severe side effects, dietary limitations, and numerous drug interactions. Nevertheless, research has demonstrated its efficacy in treating depression that is unresponsive to alternative antidepressant medications, sometimes referred to as treatment-resistant depression. Selective serotonin and norepinephrine reuptake inhibitors (SNRIs) are further regarded as a preferred initial treatment. These medications are believed to function by increasing the levels of serotonin and norepinephrine. Norepinephrine boosts vigilance and concentration. Similar to selective serotonin reuptake inhibitors (SSRIs), these drugs exactly have a delayed onset of action, typically taking 2 weeks to begin functioning and 4 to 8 weeks to reach their full medicinal benefit.

There are five well-recognized selective serotonin reuptake inhibitor (SSRI) drugs that have been licensed by the Food and Drug Administration (FDA) for the treatment of depression. These medications are Citalopram, Escitalopram, Fluoxetine, Paroxetine, and Sertraline**.** (Christina Aungst, 2024)

## 1.2.1: Limitations of Available Antidepressants

While antidepressants are generally considered safe, they are not devoid of adverse effects. A medicine can be deemed safe despite the presence of side effects, as long as these side effects are non-lethal and/or resolve upon discontinuation of the prescription. This statement holds significant validity when applied to antidepressant medications.

Some prevalent adverse effects of antidepressants include: Exhaustion Gastrointestinal discomfort Reduced sexual desire. (Margaret Seide, 2023)Antidepressants, such as SSRIs and SNRIs, elevate serotonin levels in the brain. Serotonin is a neurotransmitter which helps in the flow of chemical signals in the brain, and it is believed to contribute to the alleviation of depression symptoms. Excessive levels of serotonin can result in symptoms such as:

Uncertainty or lack of clarity, Perceptions of nonexistent sensory sensations, Ataxia Pyrexia Tachycardia , Emesis, and thrombotic reflex (Leigh Ann Anderson, 2022).

## 1.3: Drug Development Process from Medicinal Plants

Throughout history, medicinal plants have consistently shown to be the most fruitful resource for discovering potential compounds that can be developed into medications. Drug discovery encompasses a diverse methodology that integrates botanical, biological, and molecular approaches. The ongoing exploration of medicinal plants for drug discovery continues to yield innovative and significant findings in the fight against many diseases. The creation of new drugs is crucial since there is a high occurrence of various diseases for which there are no effective, dependable, and less harmful treatments available. Medicinal research plays a crucial role in the study of drug discovery for companies that manufacture drugs. Before the registration of a novel medicine, it is important to conduct a comprehensive investigation of the chemical. The screening methods employed to examine the efficacy of plant-based compounds can be carried out either by randomly picking the plant material or by identifying possible candidates through purpose-built databases. (Ojah, 2020)

## 1.4: Details of *Acanthus ilicifolious L.*

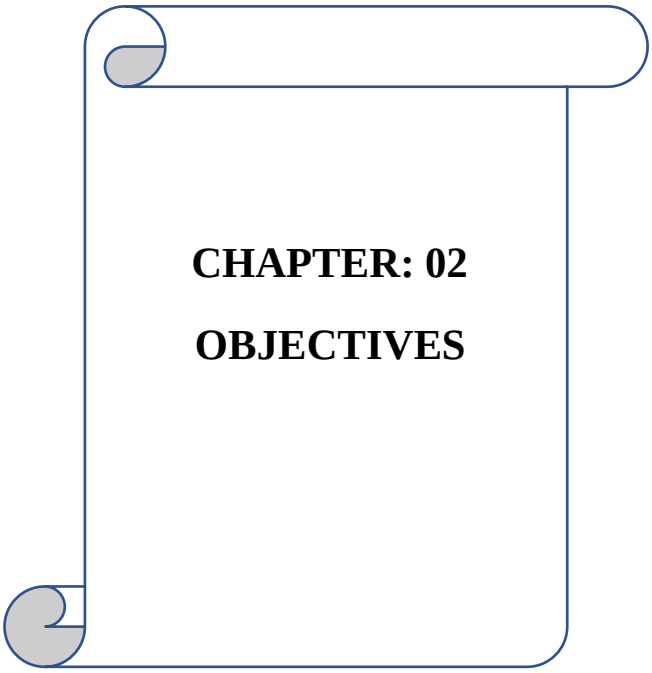
Acanthus ilicifolius, also referred to as sea holly, holly mangrove, or holly-leaved acanthus, has a long history of usage in traditional Indian and Chinese medicine. The Acanthaceae family encompasses these 1.5 m tall vines, which thrive in dense growth in the tropical regions of Asia and Africa (Naidu & Varahalarao, 2010).

In Indian Ayurveda, the A. ilicifolius species is employed as a nerve tonic, astringent, stimulant, and expectorant.

Figure 1. *Acanthus ilicifolius L.* Plant (From Shagil Kannur - Own work, CC BY-SA 4.0)

The roots of these plants are utilized for the treatment of cough, asthma, leucorrhea, and paralysis. *Acanthus ilicifolius L*. shoots and leaves are employed as a remedy for animal and insect bites. (Somorita Baishya, 2020)

Various classes of chemical compounds have been isolated and classified from *Acanthus ilicifolius*. The plant's root, leaves, aerial parts, stem, and pods have been extracted using ethanol, methanol, chloroform, and hexane. These extracts contain various chemical compounds such as alkaloids, glycosides, lignans, triterpenoid saponins, sterols, fatty acids, and coumaric acid derivatives. (Fatema Tuz Zohora1, May)



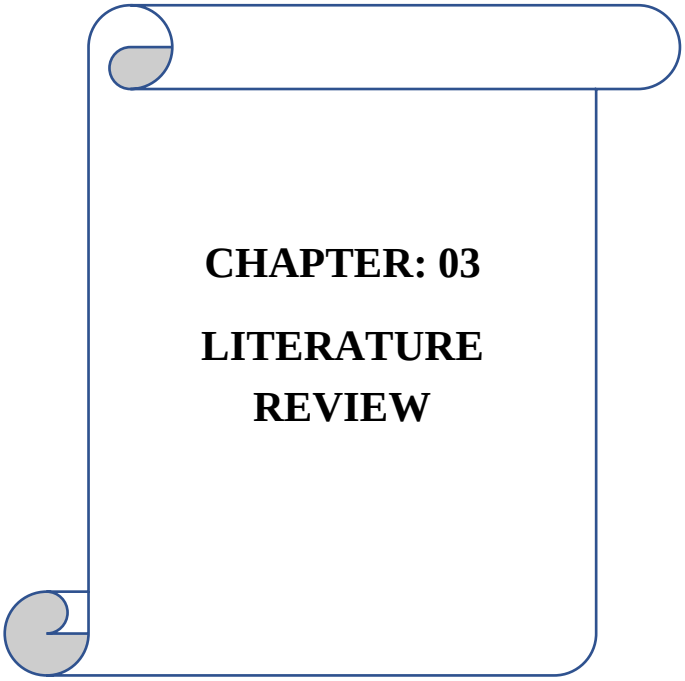
# CHAPTER: 02

# OBJECTIVES

# Chapter 02: Objectives

## 2.1: Aims and Objectives

This initiative aim of this project is to discover natural chemicals that could be used as inhibitors for the treatment of the depressive disorder. Currently, the available therapeutic choices frequently exhibit toxicity and high costs. To tackle this urgent medical requirement, the aim is to employ computational methodologies such as molecular docking, ADMET, and drug-protein binding affinity assessment to examine a collection of natural chemicals for their ability to reduce depression.



# CHAPTER: 03

# LITERATURE REVIEW

# Chapter 03: Literature Review

## 3.1: Pharmacological Activity of *Acanthus ilicifolious L.*

A variety of chemical compounds have been separated and identified from *Acanthus ilicifolius*. The plant's root, leaves, aerial parts, stem, and pods have been extracted using ethanol, methanol, chloroform, and hexane.

These extracts have been discovered to contain several chemical components. The compounds present include alkaloids, glycosides, lignans, triterpenoid saponins, sterols, fatty acids, and coumaric acid derivatives.

It is also considered to be a diuretic and is used as a cure for dropsy and bilious swellings. The plant is reported to be used in asthma. The leaves are expectorant, employed as an emollient fomentation in rheumatism and neuralgia. The plant is used for dyspepsia, paralysis, and asthma. The leaves are reported to be used in headaches, rheumatism, and skin diseases. Leaves and shoots are used as antidotes in snake bites.

Chemical substances found in *Acanthus ilicifolius L.*

### Table 1: plant part, Isolated compounds and their activities.

| Plant Part | Compounds | Activity | Reference |
|---|---|---|---|
| Leaf | 2-Benzoxazolinone | Anti-inflammatory, Anti-microbial, Antinociceptive | (https://doi.org/10.4103%2F0975-7406.106557) |
| | Apigenin-7-0-glucuronide | | |
| | Fucosterol | | |
| Root | Stigmasterol | Anti-leishmanial activity | |
| | 2-Benzoxazolinone | | |
| Whole Plant | Quercetin | Antidepressant | |
| | beta-Sitosterol | Anti-inflammatory | |

Acancifoliuside, a derivative of coumaric acid, was obtained from the methanolic extract of the leaves. The alcoholic extract of *Acanthus ilicifolius L.*, administered at doses of 250 and 500 mg/kg body weight, has shown efficacy in inhibiting tumor progression and preventing the production of cutaneous papilloma generated by carcinogens. (Aeri, 2013 ) (https://doi.org/10.4103%2F0975-7406.106557)

## 3.2: Antidepressant Activity of Quercetin

Flavonoids are a group of phenols with low molecular weight. They can be categorized into many subgroups based on their molecular structures, including flavones, flavanones, isoflavones, isoflavones, pterocarpans, coumestans, anthocyanins, flavanols (or catechins), and flavanols. The flavonoids, namely kaempferol, quercetin, and myricetin, are the most prevalent among these flavanols due to their notable functional qualities. Undoubtedly, Quercetin is a potent suppressor of lipid peroxidation, as it diminishes the activity of both cyclooxygenase and lipoxygenase. This is responsible for inhibiting the production of inflammatory metabolites. In addition, quercetin also enhances the activity of antioxidant enzymes, hence inhibiting the generation of free radicals. Additionally, it can form coordination complexes with transition metal ions. Quercetin can cross the blood-brain barrier. It can be found in the brain a few hours after being given. It has a significant impact on the central nervous system and promotes the survival of neurons. It is recognized to enhance stress-related behavioral dysfunction by reducing oxidative stress in the brain. (Serena SilvestroORCID, 2021)

### 3.2.1: Fucosterol

Fucosterol is a distinctive phytosterol generated from algae that possesses several therapeutic qualities, such as antioxidant, anti-inflammatory, anticholinesterase, and neuroprotective effects. (Md. Abdul HannanORCID, 2019)

Depression and epilepsy are prevalent neurological conditions. Individuals diagnosed with epilepsy are significantly more susceptible to experiencing signs of depression, and the incidence of suicide among epilepsy patients is considerably more than that of the general population. Cholesterol is a fundamental constituent of cell membranes in humans and plays a crucial role in the central nervous system. Furthermore, it has been observed that steroids exhibit antidepressant properties (Han, 2005). Fucosterol, a molecule found in brown algae, plays a regulatory role in genes associated with cholesterol homeostasis. Fucosterol had notable antidepressant-like effects in both the forced swim test and tail suspension test. Fucosterol is believed to exert its effects by boosting the levels of serotonin and noradrenaline in the central nervous system. This, in turn, may lead to an antidepressant-like effect. Fucosterol may achieve this by elevating central BDNF levels (Xing-Hua Zhen a, 2015).

# CHAPTER: 04
# METHODOLOGY

# Chapter o4: Methodology

## 4.1: Phytoconstituents of *Acanthus ilicifolious L.*

**Table 2: Phytoconstituents Obtained from *Acanthus ilicifolius L.*** (Acanthus ilicifolius, n.d.)

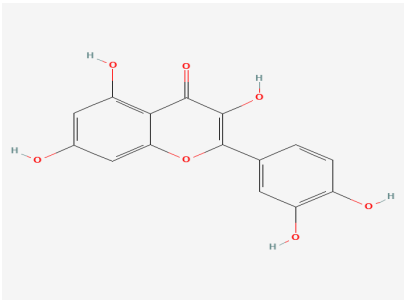
| Phytoconstituents | PubChem ID | Chemical Class |
|---|---|---|
| 2-Benzoxazolinone | 6043 | Benzo oxazolones |
| Apigenin-7-0-glucuronide | 12912214 | Flavonoid |
| Ursolic acid | 64945 | pentacyclic triterpene |
| Beta-Amyrin | 73145 | pentacyclic triterpenoid |
| Campesterol | 173183 | sterol |
| 1-Octacosanol | 68403 | fatty alcohol |
| Stigmasterol | 5280794 | tetracyclic triterpenes |
| Acanthicifoline | 442503 | Alkaloids |
| Betulin | 72326 | Prenol lipids |
| Quercetin | 5280343 | Flavonoids |
| Schottenol | 441837 | steroid |
| Cholesterol | 5997 | Steroids |
| Trigonelline | 5570 | Pyridine alkaloids |

## 4.2: Major Ligands for Antidepressant Effect

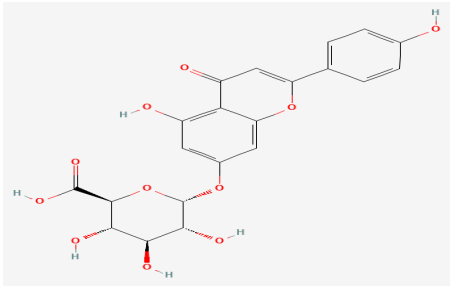
The antinociceptive action of the *Acanthus ilicifolius* plant has been demonstrated through in vivo testing. The phytochemical examination of this test has resulted in the isolation of substances such as flavonoids, alkaloids, and steroids. Within the group of isolated compounds, some ligands belonging to the flavonoid and steroid classes can be utilized as test ligands for antidepressant properties. Subsequently, modular docking can be performed in the subsequent stages. (Md. Amirul Islam, 2012)

Major Ligands for the Antidepressant Effect:

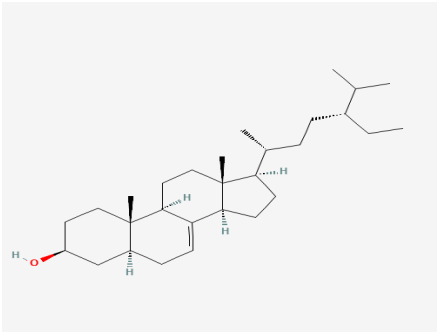
**Figure 2: Chemical Structures** (PubChem , n.d.)



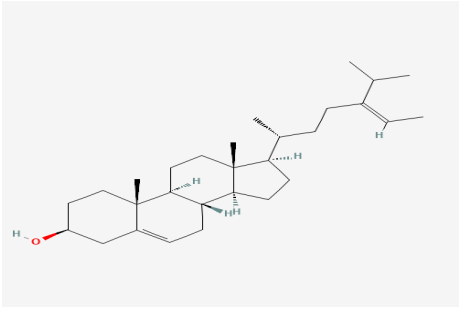
**Quercetin (PubChem ID: 5280343)**



**Apigenin-7-o-glucuronide (PubChem ID: 12912214)**



**Fucosterol (PubChem ID:5281326)**

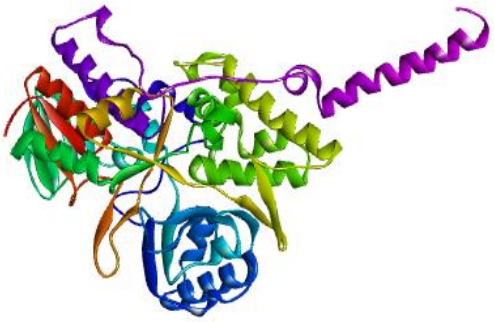


**Schottenol (PubChem ID: 441837)**

## 4.3: Receptor Preparation and Optimization

The 3D structure of Human Monoamine Oxidase A (PDB: G110A) (https://www.rcsb.org/structure/2Z5Y) in PDB format was obtained from RCSB PDB. To obtain a purified protein, it is necessary to exclude water and heteroatoms, as well as remove any ligands that are already attached to the receptor protein. Consequently, the receptor has undergone a complete transformation, resulting in a clean shape. Following the formation of the receptor, it is crucial to minimize its energy. SPDBV can be utilized to optimize the energy of the protein and assign it a new name for enhanced comprehensibility. Next, the AutoDock Tools-1.5.7 software was used to incorporate hydrogen atoms, charges, and other necessary modifications to the receptor. The modified receptor protein was then saved in. pdbqt format.

**Figure 3: Structure of The Receptor**



**3D Structure of Human Monoamine Oxidase A (PDB: G110A)**

## 4.4: Ligand Preparation and Optimization

To eliminate all components of the human monoamine oxidase A (MAOA) receptor except for the conventional ligand, the Discovery Studio software needs to be utilized. Subsequently, saved it in the .pdb format. Next, the ligand's energy was minimized by using Chimaera 1.13.1. After that, AutoDockTools-1.5.7 was used to incorporate polar hydrogens, select the Torsion option, and then save the ligand file in. pdbqt format.

## 4.5: Grid Box Setup

The docking area is established using the grid box. The grid box from AutoDockTools-1.5.7 was accessed and the binding region of the target protein and ligand was adjusted within the grid box. Subsequently, a configuration file is generated and stored under the name "conf.text"

receptor = Protein.pdbqt
ligand = harmin. pdbqt

size_x = 24
size_y = 22
size_z = 22

center_x = -40.838
center_y = -26.715
center_z = -15.206

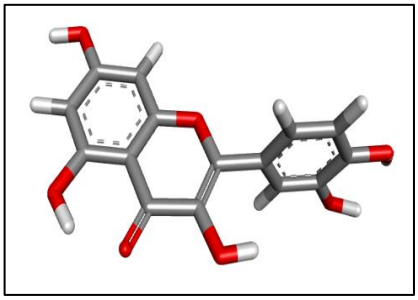
out = harmin_out.pdbqt
log = harmin.txt

energy_range = 3
num_modes = 9
exhaustiveness = 8

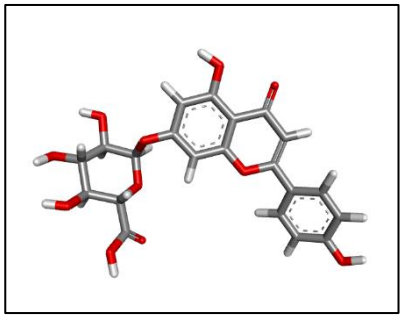
## 4.6: Test Ligands Preparation

The ligands that were previously chosen were similarly subjected to energy minimization. To do this Chimaera, 1.13.1. was utilized. Subsequently, the test ligands underwent essential adjustments using AutoDockTools-1.5.7 and then saved.Pdbqt format. For example, Ligand1.pdbqt, Ligand2.pdbqt, and so on.

**Figure 4: 3D Structures of Test Ligands**

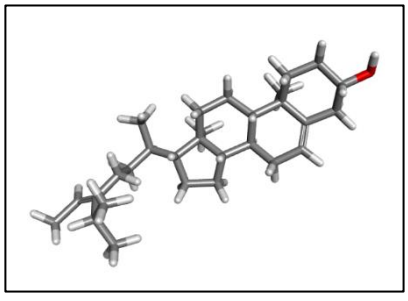


**3D Structure of Quercetin (PubChem:5280343)**



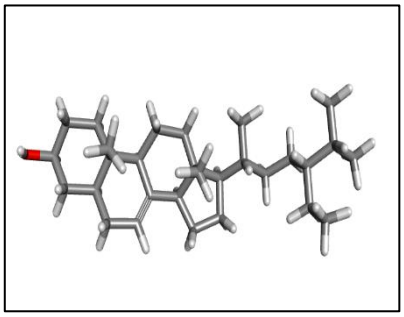
**3D Structure of Apigenin-7-0-glucuronide**

**(PubChem:12912214)**



**3D Structure of Fucosterol**

**(PubChem:5281326)**



**3D Structure of Schottenol**

**(PubChem:441837)**

## 4.7: Docking

Molecular docking is an essential tool used in structural molecular biology and computer-aided drug design. Ligand-protein docking aims to forecast the primary binding configuration(s) of a ligand with a protein that has a known three-dimensional structure**.** (Garrett M Morris 1, 2008)

Before starting the docking process, it is necessary to arrange the receptor, ligand, and configuration files within a designated folder. These three files, receptor.pdbqt, Ligand.pdbqt, and conf.text, should be stored together in a single folder. The docking process was executed using AutoDock Vina 1.1.2. Initially, the accuracy of the binding process was assessed by re-docking the standard receptor Human Monoamine Oxidase A and the standard ligand Harmin. Subsequently, the binding affinity values can be compared by sequentially docking the test ligands.

## 4.8: ADMET Analysis

ADMET, which stands for chemical absorption, distribution, metabolism, excretion, and toxicity, plays a crucial role in the process of drug discovery and development. An ideal drug candidate must possess both potent efficacy against the therapeutic target and suitable ADMET characteristics at a therapeutic dosage. Many in silico models are created specifically for predicting chemical ADMET characteristics. (ADMET-score – a comprehensive scoring function for evaluation of chemical drug-likeness†, 2019 )

pkCSM software was used for ADMET analysis. (https://biosig.lab.uq.edu.au/pkcsm/)

# CHAPTER: 05

# RESULT AND DISCUSSION

# Chapter 05: Result and Discussion

## 5.1: Validation of Docking

The results of previous docking and subsequent re-docking are highly proximate. The re-docking results demonstrate that the drug-protein binds to the identical amino acid at the exact location. The RMSD value obtained from the re-docking was compared to the standard value to verify the accuracy of the docking technique. Upon re-docking, the root-mean-square deviation (RMSD) value was determined to be 0.565 angstrom, which is below the minimum value of 2 angstrom. Therefore, it can be accepted that the docking process is accurate.

## 5.2: Test Ligands and Proteins Interaction Analysis

Interactions between 4 test ligands (Ligand 1: Quercetin, Ligand 2: Apigenin-7-0-glucuronide, Ligand 3: Fucosterol, Ligand 4: Schottenol) and target proteins were observed.

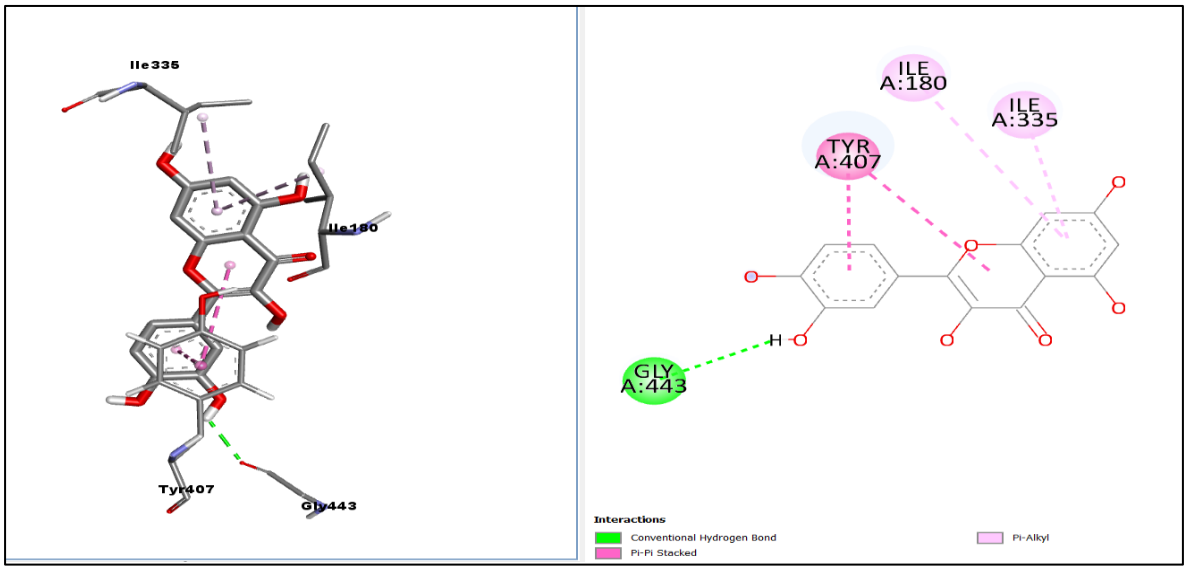



**Figure 5.1:** 3D and 2D structure of receptor-ligand1 interactions (-9.6 kcal/mol)

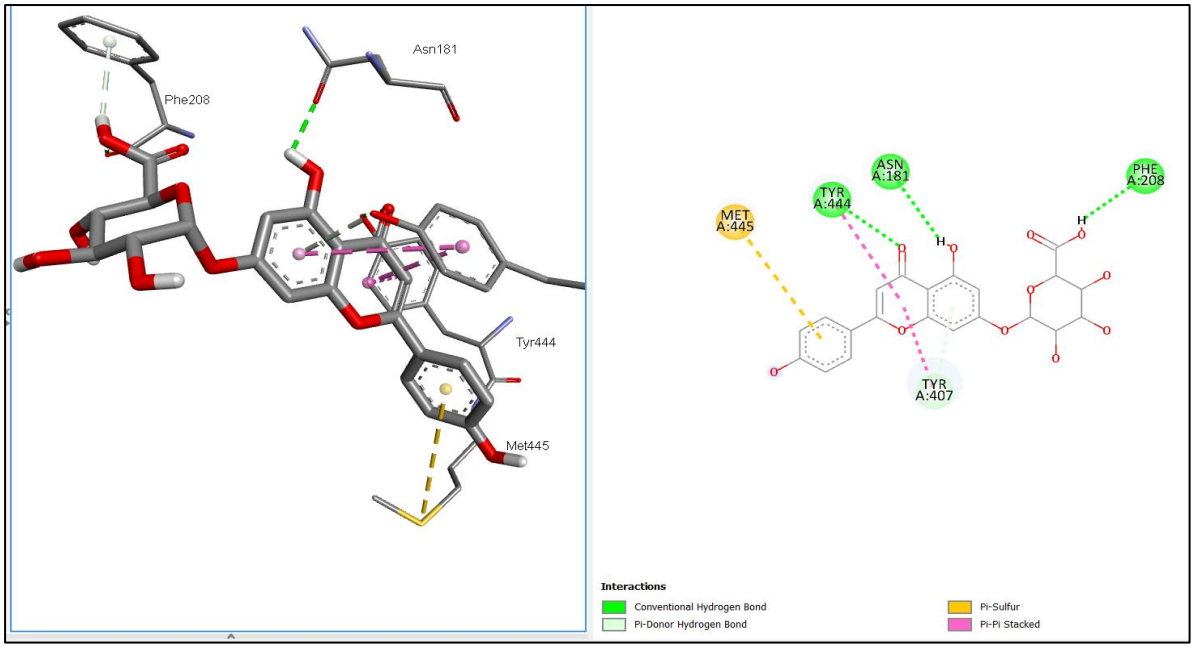



**Figure 5.2:** 3D and 2D structure of receptor-ligand2 interactions (-7.9 kcal/mol)

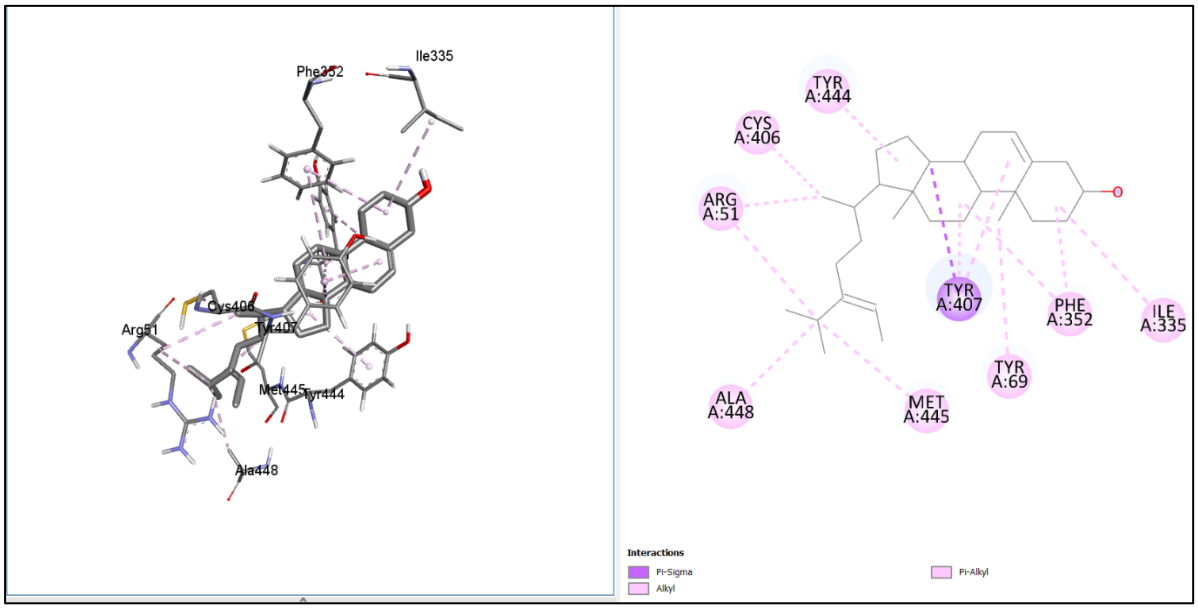



**Figure 5.3:** 3D and 2D structure of receptor-ligand3 interactions (-7.8 kcal/mol)

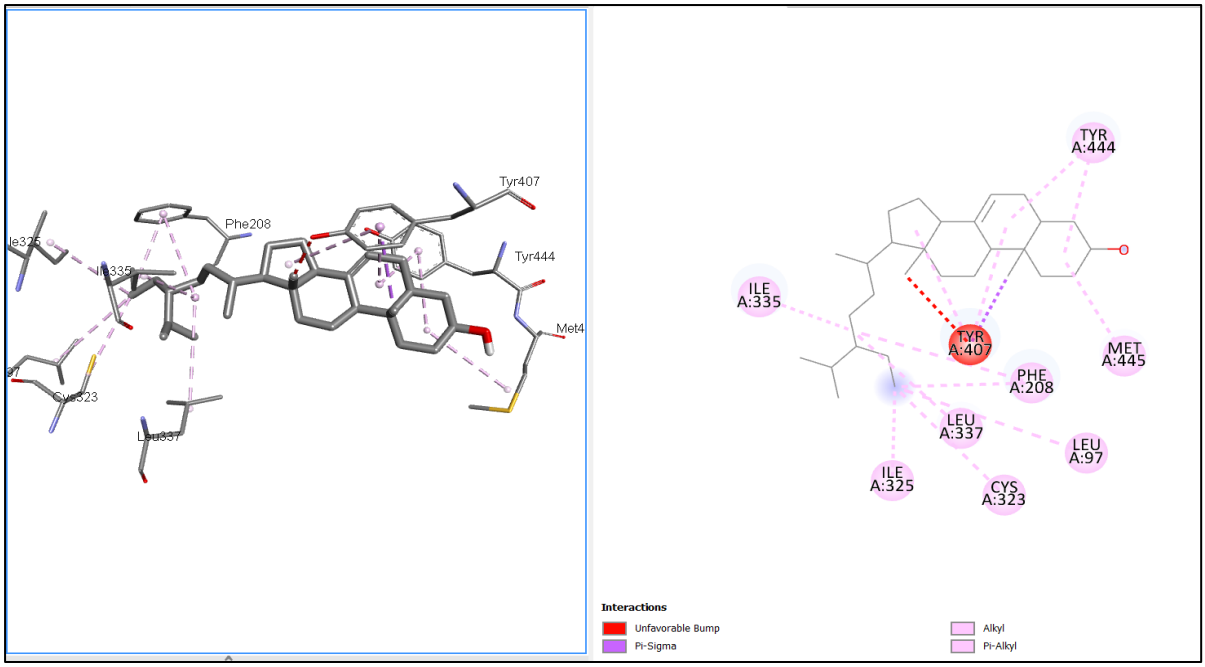



**Figure 5.4:** interactions 3D and 2D structure of receptor-ligand4 (-7.9 kcal/mol)

The 2D and 3D structures in the pictures illustrate the binding and interaction of the 4 test ligands with the receptor. The structures also revealed the accurate binding locations of amino acids that displayed binding affinities comparable to or greater than those of the standard.

Four test ligands were selected for screening against the target. All of them exhibited outcomes that were either equivalent to or superior to the standard after the process of docking.

The 3D and 2D presentations demonstrate the existence of hydrogen bonds in Quercetin and Apigenin-7-0-glucuronide, which were not present in the standard. Hydrogen bonds are essential to influencing the effectiveness of ligand binding.

# Table 3. Receptor-Legends Binding Affinity

| Ligand Number | Ligand Name | Pub Chem | Binding Affinity (kcal/mol) | Hydrophobic Interaction | Hydrogen Bond | RMSD Value |
|---|---|---|---|---|---|---|
| | Harmine | 5280943 | -8.5 | ILE180, ASN181, PHE208, GLN215, CYS323, ILE335, LEU337, PHE352, TYR407, TYR444 | | 0.565 |
| 1 | Quercetin | 5280343 | -9.6 | TYR407, ILE180, GLN215, ILE335, PHE352 | GLY443 | H-Bond distance 4.46 |
| 2 | Apigenin-7-0-glucuronide | 12912214 | -7.9 | MET445, TYR407 | PHE208, TYR444, ASN181 | H-Bond Distance 2.48, 5.07, 3.58 |
| 3 | Fucosterol | 5281326 | -7.8 | TYR444, CYS406, ARG51, TYR407, ALA448, PHE352, ILE335, MET445 | | |
| 4 | Schottenol | 441837 | -7.9 | ILE335, MET445, LEU97, LEU337, PHE208, ILE325, TRY444, TYR407 | | |

As a result of the test ligands exhibiting a reasonably high affinity in comparison to the standard, it is advisable to include these ligands in the subsequent drug discovery phase as potential antidepressant drugs. This is because natural ligands are more inclined to have a reduced occurrence of adverse effects.

## 5.3: ADMET Data Prediction (Douglas E. V. Pires, 2015)

| CID | Absorption | | | Distribution | | Metabolism | | Excretion | | Toxicity | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Water Solubility | Caco2 Permeability | Intestinal Absorption | VDss(Human) | BBB Permeability | CYP 2C19 Inhibitor | CYP 2D6 Substrate | Total Clearance | Renal OCT2 Substrate | ADMES Toxicity | Skin Sensitization | Hepatotoxicity |
| 5280343 | -2.925 | -0.229 | 77.207 | 1.559 | -1.098 | No | No | 0.407 | No | No | No | No |
| 12912214 | -2.762 | -0.693 | 15.25 | 0.319 | -1.305 | No | No | 0.588 | No | No | No | No |
| 5281326 | -6.715 | 1.212 | 94.64 | 0.179 | 0.764 | No | No | 0.619 | No | No | No | No |
| 441837 | -6.773 | 1.201 | 94.46 | 0.193 | 0.781 | No | No | o.621 | No | No | No | No |

The ADMET chart predicts the values of several variables related to the absorption, distribution, metabolism, excretion, and toxicity of test ligands. Based on these data, it may be inferred that the ligands do not exhibit any harmful effects such as hepatotoxicity or skin sensitization. The absorption figures suggest that the test ligands come out within the absorption rate range of 70-90. The table above provides essential values for distribution, metabolism, and excretion, which might be utilized for future drug research.

# CHAPTER: 06

# CONCLUSION

# Chapter 06: Conclusion

Currently, Depressive Disorders are rapidly emerging as a global menace. Nowadays, research is underway to discover drugs that are both safer and more effective, as well as to develop new anti-depressant medications with improved clinical attributes.

IMPPAT was used to obtain a list of phytochemicals from *Acanthus ilicifolious*. A computational screening of the small chemical library was performed to determine the specific biological targets responsible for the anti-depressant effects.

40% of the ligands used in the in silico molecular docking tests achieved docking scores that were equivalent to or higher than the standard. This suggests the potential for discovering and creating new antidepressant medications in the future. *Acanthus ilicifolious L*. has the potential to serve as a valuable natural resource in the development of innovative anti-depressant drugs.

# CHAPTER: 07

# REFERENCE

# Chapter 07: Reference

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