TO EVALUATE THE ANTI-DEPRESSANT ACTIVITY OF ETHANOLIC LEAF EXTRACT OF HIBISCUS ROSA SINENSIS IN RAT

Mr., Vivek Maurya

Dr. Abhay Pratap Yadav

Miss. Shivanki Verma

Mr. Vijay Maurya

RK Pharmacy College Azamgarh

Vivekpharma2000@gmail.com

ABSTRACT

Aim: To evaluate the Anti-Depressant Activity of Ethanolic Leaf Extract of Hibiscus Rosa Sinensis in Rat.

Study design: 'Soxhlation' continuous hot percolation was used for the extraction process. Hibiscus rosa sinensis leaves that had been dried and ground up were put in the Soxhlet thimble. At first, soxhlation was carried out at 60 °C using Petroleum ether as a non-polar solvent. Plant waste (marc) was dried before being extracted with ethanol. Soxhlation was continued for each solvent until no color was seen in the siphon tube. The swim despair test and Hibiscusrosa sinensis (HRS) at doses of 50 mg/kg and 100 mg/kg. The benchmark was floxetine (10mg/kg, body weight). In both two doses, a significant dose-dependent reduction in immobility time was noted. HRS extract was used to measure MAO activity, and the results showed that each dose of this plant had a noticeable impact on MAO, with a considerable effect at 100mg/kg.

Methodology: We utilize male Sprague-Dawley rats that weigh between 160 and 180 g. At least a day before the experiment, they are brought to the lab where they are kept apart in Makrolon cages with unrestricted access to food and water. We utilize male Sprague-Dawley rats that weigh between 160 and 180 g. At least a day before the experiment, they are brought to the lab where they are kept apart in Makrolon cages with unrestricted access to food and water. We utilize male Sprague-Dawley rats that weigh between 160 and 180 g. At least a day before the experiment, they are brought to the lab where they are kept apart in Makrolon cages with unrestricted access to food and water. After two to three minutes, activity starts to slow down and is broken up by longer periods of floating or immobility. The rats become immobilized for 80% of the time after the first 5–6 minutes of immobility. The rats are taken out of the water after 15 minutes and allowed to dry in a heated enclosure (32 °C) before being put back in their original cages. After 24 hours, they are placed in the cylinder once more, and a 5-minute test is used to determine the total amount of time they were immobile.

Results: Fluoxetine (10mg/kg) was given to rats as a positive control, and it considerably reduced immobility time (85.01.88) as compared to the control group. While HRS extract (50 mg/kg and 100 mg/kg) markedly reduced immobility time (65.0.74 and 70.2.84, respectively).

Conclusion: The immobility is assumed to be caused by either the development of a passive behavior, which means the animal has lost the ability to deal with stressful stimuli, or the persistence of escape-directed behavior (also known as despair behavior). Based on the findings, it was determined that the ethanolic HRS extract had considerable antidepressant action at both the 50 mg/kg and 100 mg/kg doses.

Keywords: Antidepressants, monoamine oxidase, Hibiscusrosa sinensis, fluoxetine.

INTRODUCTION

DEPRESSION

Depression is a mental health disorder characterized by persistent feelings of sadness, hopelessness, and a loss of interest or pleasure in activities. It affects how a person thinks, feels, and behaves and can significantly impact their daily functioning, relationships, and overall quality of life^{.[1]}

Depression is classified as a mood disorder characterized by a continual state of sadness and diminished interest. Referred to as major depressive disorder or clinical depression, it significantly impacts one's emotional, cognitive, and behavioral aspects, potentially resulting in a range of psychological and physiological complications. Engaging in routine daily activities may become challenging, and at times, an individual may experience a sense of life's insignificance.^[2]

TYPES OF DEPRESSION

Depression can manifest in different forms, and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) outlines several specific types of depression. It's important to note that individuals can experience different types of depression at different times in their lives, and the severity and duration of symptoms may vary. Here are some common types of depression ^[3]:

- **Major Depressive Disorder (MDD):** Major Depressive Disorder, alternatively referred to as clinical depression, stands as the prevailing and widely recognized manifestation of depression.
- **Persistent Depressive Disorder (PDD):** The symptoms of PDD are milder compared to MDD but are persistent and can interfere with daily functioning. People with PDD may experience a lack of interest or pleasure, changes in appetite, sleep disturbances, low energy, poor self-esteem, difficulty making decisions, and feelings of hopelessness⁻
- Seasonal Affective Disorder (SAD): A kind of depression known as seasonal affective disorder often manifests in the fall and winter when there is less natural sunlight.
- **Postpartum Depression (PPD):** Postpartum Depression is a condition that affects women subsequent to childbirth, and is typified by profound emotions of melancholy, apprehension, and fatigue.

- **Bipolar Disorder:** Bipolar Disorder, formerly known as manic-depressive disorder, is not solely a depressive disorder but involves reckless behavior, and a decreased need for sleep during the manic or hypomanic phase.
- **Psychotic Depression:** Psychotic Depression is a severe form of depression characterized by the presence of psychotic symptoms alongside depressive symptoms.

SYMPTOMS OF DEPRESSION

• **Persistent Sadness:** Feelings of sadness, emptiness, or hopelessness that persist for most of theday, nearly every day. This sadness is different from normal feelings of sadness that arise fromspecific events and tends to linger for an extended period ^[4].

• Loss of Interest or Pleasure: A significant decrease or complete loss of interest or pleasure inactivities that were once enjoyable, including hobbies, socializing, or engaging in previouslysatisfying activities. This symptom is known as anhedonia.

• **Changes in Appetite and Weight**: Significant changes in appetite, resulting in noticeable weight loss or weight gain. Some individuals with depression may experience a loss of appetite, leading to unintentional weight loss, while others may experience an increase in appetite and subsequent weight gain ^[5].

• Sleep Disturbances: Changes in sleep patterns, such as insomnia (difficulty falling asleep or staying asleep) or hypersomnia (excessive sleepiness or prolonged sleep). Depression can disrupt the normal sleep-wake cycle, leading to difficulties in getting adequate restful sleep.

• **Fatigue and Lack of Energy**: Persistent feelings of fatigue, low energy levels, and a general sense of being physically and mentally drained. Individuals with depression often find even simple tasks to be exhausting and may struggle to muster the energy to carry out daily activities.

• **Feelings of Worthlessness or Guilt:** A pervasive sense of worthlessness, excessive guilt, or self-blame. People with depression often have negative self-perceptions, feel excessively responsible for negative events, and believe they are a burden to others.

• **Difficulty Concentrating and Making Decisions**: Cognitive symptoms are common in depression, including difficulties with concentration.

• **Restlessness or Slowed Movement:** Restlessness, agitation, or an inability to sit still, known as psychomotor agitation, may be present in some individuals with depression. On the other hand, depression can also lead to psychomotor retardation, where there is a significant slowingdown of physical and mental processes⁻

• **Suicidal Thoughts**: In severe cases of depression, individuals may experience recurring thoughts of death, suicidal ideation, or engage in self-harming behaviors ^[6].

CAUSES AND RISK FACTORS:

- **Genetic Factors:** There exists substantial evidence indicating the involvement of genetics in the onset of depression. Individuals possessing a familial background of depression face an elevated susceptibility to developing the condition themselves ^[7].
- **Neurochemical Imbalances:** Neurotransmitters serve as chemical messengers within the brain, playing a crucial role in the regulation of mood, emotions, and overall brain function.
- **Changes in Brain Structure and Function**: Research has shown that individuals with depression may have alterations in brain structure and function. These changes can involve areas of the brain responsible for mood regulation, such as the prefrontal cortex, hippocampus, and amygdale ^[8].

TREATMENT OF DEPRESSION

Depression is a treatable condition, and several effective treatment options are available. The choice of treatment depends on the severity of symptoms, individual preferences, and the presence of any underlying conditions ^[9].

1. Psychotherapy: Psychotherapy, also known as talk therapy or counseling, is a fundamental treatment approach for depression. Different types of psychotherapy may be used, including ^[10]:

• **Cognitive Behavioral Therapy** (**CBT**): CBT helps individuals identify negative thought and. It focuses on changing distorted thinking patterns that contribute to depression and encourages positive behaviorchanges.

• **Interpersonal Therapy (IPT):** IPT focuses on improving interpersonal relationships and addressing social and relationship issues that may be contributing to depression. It helps individuals develop better communication skills, resolve conflicts, and enhance their support systems.

• **Psychodynamic Therapy:** This form of therapy explores unconscious patterns and unresolved conflicts that may be contributing to depression. It aims to increase self-awareness and understanding of how past experiences may be influencing current emotions and behaviors.

- **2. Medication:** Antidepressant medications can be prescribed help alleviate depressive symptoms ^[11].
 - Selective Serotonin Reuptake Inhibitors (SSRIs)- Examples: Fluoxetine (Prozac), Sertraline (Zoloft), Escitalopram (Lexapro)
 - Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)- Examples: Venlafaxine (Effexor), Duloxetine (Cymbalta), Desvenlafaxine (Pristiq)
 - Tricyclic Antidepressants (TCAs) Examples: Amitriptyline (Elavil), Nortriptyline (Pamelor), Fluvoxetine (Tofranil)
 - Monoamine Oxidase Inhibitors (MAOIs) Examples: Phenelzine (Nardil), Tranylcypromine (Parnate), Isocarboxazid (Marplan)
 - Atypical antidepressant Examples: Bupropion (Wellbutrin), Mirtazapine (Remeron), Trazodone (Desyrel)

3. Brain Stimulation Therapies: In cases where psychotherapy and medication have not been effective, or if the depression is severe, brain stimulation therapies may be considered. These include ^[12]:

• **Electroconvulsive Therapy (ECT):** ECT involves delivering controlled electric currents to the brain, which induces a brief seizure. It is generally ECT is conducted under anesthesia and closely monitored by a healthcare professional.

• **Transcranial Magnetic Stimulation (TMS):** TMS uses magnetic fields to stimulate specific areas of the brain associated with mood regulation. It is a non-invasive procedure that is typically conducted on an outpatient basis.

4. Lifestyle Changes: Certain lifestyle modifications can complement other treatment approaches and help manage depressive symptoms. These may include ^[13]:

• **Regular exercise:** Engaging in physical activity, such as walking, jogging, or yoga, has been shown to improve mood and reduce symptoms of depression⁻

• **Healthy diet**: A balanced diet rich in fruits, vegetables, whole grains, lean proteins, and omega-3 fatty acids may have a positive impact on mood and overall well-being[.]

• **Sufficient sleep**: Establishing good sleep hygiene and ensuring adequate sleep can improve mood and mental health[.]

• **Stress management**: Learning and practicing stress reduction techniques, such as mindfulness meditation, deep breathing exercises, or relaxation techniques, can help manage stress and promote emotional well-being⁻

• **Social support:** Building and maintaining a strong support system of family, friends, or support groups can provide emotional support and alleviate feelings of isolation.

NEUROTRANSMITTERS INVOLVED IN ANTIDEPRESSANT ACTIVITY

Norepinephrine: Norepinephrine (also known as noradrenaline) is a neurotransmitter involved in the body's stress response and arousal. It plays a role in regulating attention, alertness, and mood ^[14].

Dopamine: Dopamine is a neurotransmitter associated with motivation, reward, and pleasure. It plays a role in regulating mood, motivation, and movement. Although dopamine is primarily associated with conditions like Parkinson's disease and addiction, it also has implications for depression.

Gamma-Aminobutyric Acid (GABA): GABA is an inhibitory neurotransmitter that helps regulate neuronal activity. It has a calming effect on the brain and helps reduce anxiety and stress. While the exact role of GABA in depression is still being investigated, some studies suggest thatGABAergic dysfunction may contribute to depressive symptoms ^[15].

Glutamate: Glutamate is the primary excitatory neurotransmitter in the brain. It is involved in various brain functions, including learning, memory, and mood regulation.

Endogenous Opioids: Endogenous opioids, such as endorphins, enkephalins, and dynorphins, are natural pain-relieving substances produced by the body. They also play a role in regulating mood, stress, and reward pathways.

Serotonin: The serotonin hypothesis of depression suggests that a deficiency or imbalance of serotonin contributes to the development of depressive symptoms. It proposes that low levels of serotonin in certain brain regions, such as the prefrontal cortex and limbic system, may impair mood regulation and lead to depressive symptoms ^[16].

PLANT DESCRIPTION

Hibiscus rosa sinensis, commonly known as the Chinese hibiscus or shoeblackplant, is a flowering plant that belongs to the family Malvaceae. It is native to East Asia, including China and India, butis now cultivated in many tropical and subtropical regions worldwide for its ornamental beauty. Here is a profile of the *Hibiscus rosa sinensis* plant ^[17].



Fig: - 1- Hibiscus rosa-sinensis Scientific classification

Table: - 1- classification of plant		
Kingdom:	Plantae	
Clade:	Tracheophytes	
Clade:	Angiosperms	
Clade:	Eudicots	
Clade:	Rosids	
Order:	Malvales	
Family:	Malvaceae	
Subfamily:	Malvoideae	

Tribe:	Hibisceae
Genus:	Hibiscus
Species:	H. rosa-sinensis

USES OF HIBISCUS ROSA SINESIS:

Hibiscus rosa sinensis has a long history of traditional medicinal use. Various parts of the plant, including the flowers, leaves, and roots, are used to prepare herbal remedies. The flowers and leaves are often used to make herbal teas or infusions that are believed to have various health benefits. Hibiscus tea is known for its potential antioxidant properties and is consumed for its potential effects on blood pressure, cholesterol levels, and overall cardiovascular health. Apart from its ornamental and medicinal uses, *Hibiscus rosa sinensis* is also used in the cosmetic industry. The flowers are sometimes used in the production of natural hair care products and hair dyes. Additionally, the plant is known to attract pollinators such as butterflies and hummingbirds, making it a desirable choice for butterfly gardens or wildlife-friendly landscapes ^[18].

MATERIAL AND METHOD

Collection and Authentication of the Plant

Hibiscus rosa sinensis Leaf plant was collected from R. K. P. C. Hebal Garden Kashipur surai, sathioan, Azamgarh Uttar Pradesh. And plant authenticate by Prof. Nawal Kishor Dubey, Department of Botany, Banaras Hindu University Varanasi, India, approved the plant voucher's specimen no. malva 2023/01.

Experimental Animal

Sprague–Dawley (SD) rats (weighing 220–250 g) were kept under a 12-h day-night cycle at 20°C and a relative humidity of 50% for 7 days. These SD rats were fasted but allowed free access to water for 12 h prior to each experiment. Sprague–Dawley rats of both sexes, 10–12 weeks old, were allowed access to commercial rat chow pellets and drinking water *ad libitum*. They were housed under standard conditions of controlled temperature, humidity and light and dark cycles.

Extraction

'Soxhlation' continuous hot percolation was used for the extraction process. Hibiscus rosa sinensis dried, pulverized leaves were put in the Soxhlet apparatus thimble. Petroleum ether was initially used as a non-polar solvent for soxhlation, which was done at a temperature of 60 °C. Plant waste (marc) was dried before being extracted with ethanol. Soxhlation was continued for each solvent until no color was seen in the siphon tube. Colorless solvent was gathered from the siphon tube and evaporated for residue in order to validate that the plant marc had been drained (i.e., that the extraction was finished). The absence of residue indicated that the extraction was successful. Utilizing a rotary vacuum evaporator (Bucchi type) set at 40°C, obtained extracts were evaporated. The formula was used to determine the extractive value ^[19].

DESPAIR SWIM TEST

We utilize male Sprague-Dawley rats that weigh between 160 and 180 g. At least a day before the experiment, they are brought to the lab where they are kept apart in Makrolon cages with free access to food and water. Individually, untrained rats are made to swim inside a vertical Plexiglas cylinder that is 40 cm tall, 18 cm wide, and contains 15 cm of water that is kept at 25 °C. When rats are first placed in the cylinders, they are immediately very active and will swim erratically in circles, try to climb the wall, or dive to the bottom. After two to three minutes, activity starts to slow down and is broken up by longer periods of floating or immobility. The rats become immobile for about 80% of the time after 5-6 minutes of immobility has reached a plateau. The rats are taken out of the water after 15 minutes and allowed to dry in a heated enclosure (32 °C) before being put back in their original cages. After 24 hours, they are re-inserted into the cylinder, and a 5-minute test is used to determine how long they were immobile for overall. It has been discovered that floating behavior during this 5-minute window is repeatable among rat groups. When an animal stays passively floating in the water with its nose just above the surface and its body slightly bent but upright, it is deemed to be immobile. A standard or test medication is given an hour before the test. Fluvoxetine was chosen for the experiment because tests with the conventional medication revealed that injections given 1, 5, and 24 hours previous to the test produced the most consistent results in minimizing floating ^[20-21].

PHYTOCHEMICAL TEST

S.No	Chemical Tests	Hibiscus rosa sinensis Leaf extract
1.	Tests for Steroids and Triterpenoids:	
	Liebermann's Burchard Test	-
	Salkowski Test	-
2.	Test for Saponins:	
	Foam Test	-
3.	Tests for Alkaloids:	
	Hager's Test	+
	Mayer's Test	+
4.	Tests for Glycosides:	
	Borntrager's Test	-
	Keller Killiani Test	-
5.	Tests for Tannins and Phenolic compounds:	
	Gelatin Test	+

Tab: - 2- Hibiscus rosa sinensis Leaf extract were undergone for chemical test

	Ferric Chloride Test	+	
	Lead Acetate Test	+	
	Dilute Nitric acid Test	-	
6.	Tests for Flavonoids:		
	Ferric chloride Test	-	
	• Alkaline reagent Test	-	
	Lead acetate Test	-	
7.	Tests for Proteins:		
	• Biuret Test	+	
	Xanthoproteic Test	+	

+" present "-" absent

Pharmacological screening

Tab: -3- The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on immobility time in theDespair Swim Test In Rat

Groups	Groups	Immobility time (sec)
Groups-1	Control Group	125
Groups-2	Standard (Fluvoxetine)	Group 85
Groups-3	Low Dose Treated	65
Groups-4	High Dose Treated	70



Fig: -2- The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on immobility time in theDespair Swim Test In Rat

Tab: -4- The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on struggling time in theDespair Swim Test In Rat

Groups	Groups	Struggling time (sec)
Groups-1	Control Group	25
Groups-2	Standard (Fluvoxetine)	Group 55
Groups-3	Low Dose Treated	35
Groups-4	High Dose Treated	40



Fig: -3- The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on struggling time in theDespair Swim Test In Rat

Tab: -5-The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on the Swimming timeIn Rat

Groups	Groups	Swimming time (sec)
Groups-1	Control Group	82
Groups-2	StandardGroup(Fluvoxetine)	98
Groups-3	Low Dose Treated	75
Groups-4	High Dose Treated	85



Fig: -4-The effects of the *Hibiscus rosa sinensis* Leaf extract and treatment on the Swimming timeIn Rat in Despair Swim Test

DISCUSSION

Depression is a psychological condition marked by poor mood and reluctance to exertion. It affects over 280 million individuals of all ages, or roughly 3.5% of the world's population. Depression has an impact on a person's thoughts, actions, emotions, and general sense of wellbeing. People who are depressed frequently experience diminished pleasure or joy from activities that would otherwise make them happy or joyful, as well as loss of drive or interest in those activities. Some mood disorders, including major depressive disorder and dysthymia, can cause depressed mood as a symptom. In addition to being a transient, natural response to stressful life events like the death of a loved one, it can also be a sign of some physical illnesses and a negative side effect of certain medications and medical procedures. Sadness, trouble concentrating and thinking clearly, as well as a substantial change in food or sleep schedule, may be present. People who are depressed may feel defeated or hopeless and may think of taking their own lives. Long term or short term options are available.

A complex, chronic, and potentially fatal condition, depression is quite common all throughout the world. There have been reports of varying degrees of oxidative stress and a decline in antioxidant enzymes in people with serious depression. Studies have shown that some antidepressants can enhance internal antioxidants and decrease various oxidative stress markers. Antidepressants currently come in close to 30 different varieties. In essence, these medications have negative effects because of how they affect different neuromediators. Researchers are now looking into natural substances derived from plants because of the various negative effects of artificial antidepressants.

Hibiscus rosa sinensis, commonly known as Chinese hibiscus, is primarily known for its ornamental beauty and potential medicinal uses, particularly in relation to cardiovascular

health. However, its specific effects on depression have not been extensively studied. It is important to note that depression is a complex mental health condition that typically requires a comprehensive approach involving medical professionals.

SUMMARY & CONCLUSION

We summarized these points from study:

• *Hibiscus rosa sinensis* Leaf extract is a semi-solid extract with a deep red color. It has a slightly tangy odor and a slightly acidic taste, providing a unique sensory experience. These physical characteristics make hibiscus Leaf extract visually appealing and offer a pleasant sensory experience when consumed or used in various applications.

• In summary, the chemical tests indicate that *Hibiscus rosa sinensis* Leaf extract tested negative for steroids, triterpenoids, saponins, glycosides, flavonoids, and carbohydrates. However, it tested positive for alkaloids and proteins. Additionally, it showed positive results for tannins and phenolic compounds, as indicated by the Gelatin Test, Ferric ChlorideTest, and Lead Acetate Test. These chemical tests provide insights into the presence or absence of specific chemical constituents in the extract, which contribute to its potential medicinal and biological activities.

• Treatment with *Hibiscus rosa sinensis* Leaf extract, both at low and high doses, resulted in a decrease in immobility time in the Despair Swim Test in rats. This indicates the potential antidepressant-like effects of the extract, with the low dose showing a greater reduction in immobility time compared to the high dose. However, the immobility times were still higher than the standard group treated with Fluvoxetine.

• Treatment with *Hibiscus rosa sinensis* Leaf extract, both at low and high doses, had varying effects on struggling time in the Despair Swim Test in rats. The low dose treatment increased the struggling time, potentially indicating a decrease in despair-like behavior. However, the high dose treatment showed a lesser increase in struggling time compared to the low dose. The standard group treated with Fluvoxetine exhibited the highest struggling time, indicating its efficacy as an antidepressant in this test.

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