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Research Article

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Phytochemical and Pharmacological Investigation of the Antidepressant Activity of roots of *Rhodiola rosea*

Ankush Pandey[1*], Sachin K Jain[2], Sudha Vengurlekar[2]

[1]Research Scholar, Oriental University, Near Aurobindo Hospital sanwer Road Indore MP India 453555
[2]Faculty of Pharmacy, Oriental University, Near Aurobindo Hospital sanwer Road Indore MP India 453555
Corresponding author email: ankushpharmacy234@gmail.com

Abstract Our goal is to investigate the potential of medicinal plants in the management of depression, as all synthetic medications now available for the treatment of depression have a variety of negative effects linked to hazardous interactions. The current research is suggested the existence of additional phytochemical elements in *Rhodiola rosea* roots gives them a more effective action for managing depression, which justifies the suggested effort. The application of MeOH to *Rhodiola rosea* roots at effective doses ranging from 150 mg to 300 mg resulted in a noteworthy impact on the immobility period of all animals in various groups. The highest reported impact was 300 mg/kg b.wt. Permitted a decrease in the amount of time spent immobile in comparison to antidepressants like amitriptyline and fluoxetine. Thus, it was determined that the ethanolic extract of *Rhodiola rosea* roots, at an effective dose supported by the current investigation, could cure depression caused in mice and humans alike.

Keywords *Rhodiola rosea,* Phytochemical, Ethanolic extract, Depression

Introduction

Everyone experiences sadness from time to time. However, these emotions often pass within a few days. Depression hurts and interferes with your everyday life, as well as the lives of others around you. These days, depression is a prevalent but dangerous illness. Depression ranks fourth in the world in terms of illness burden, affecting 17–20% of the population and causing significant social and economic issues. Thankfully, there is a remedy for it as well. It may raise the chance of both emotional and a range of medical issues. Additionally, it may make it difficult for you to go about your everyday business at work or home. There are two types of depression, namely Unipolar depression and Bipolar depression

Unipolar depression: This type of depression is very common (approx 75% of the cases), non familial and mood are always swing in same direction. It is clearly associated stressful life events. Anxiety and agitation are the most common symptoms of unipolar depression.

Bipolar depression: It has a well-known pattern and is also referred to as endogenous depression. It manifests in early adulthood, is unrelated to outside stressors, and is characterized by manic and fluctuating depressive symptoms. According to the World Health Organization, mental health is characterized by an individual's ability to recognize their own skills, cope with everyday stressors, perform efficiently, and perhaps make a positive contribution to their society. This concept of mental health includes pleasant emotions and functioning as essential components of mental well-being in addition to the absence of mental disease. It is challenging to reconcile the idea that well-being is a crucial component of mental health with the variety of difficult life circumstances in which well-

being may even be unhealthy. For example, most people would view as mentally unhealthy someone who is experiencing a state of well-being while murdering multiple people in a war, and as healthy someone who is feeling desperate after losing their job in an environment with few career opportunities [1]. Many academics employ the idea of mental health, which recognizes three components of mental health: emotional well-being, psychological well-being, and social well-being. It also incorporates both crucial elements of the WHO definition, namely happy emotions and positive work productivity. Social well-being refers to positive and productive social functioning, such as social contribution, social integration, social actualization, and that social coherence. Psychological well-being includes personality traits, responsibility management skills, good relationships, and communication skills, as well as a satisfied and happy life. Emotional well-being includes cheeriness, positivity, interest in life, and satisfaction.

Material and Methods

Collection and authentication of plant material: The selected plant material ***Rhodiola rosea*** roots were collected from local area of Indore, (M. P.) India, and authenticated by botanist.

Prelimnary phytochemical analysis of extracts: Qualitative assessment as Any plant species' phytochemical analysis is an essential process as it provides first information on the existence of various chemical constituents and also opens up new avenues for investigation into the particular plant species in the future. To identify the existence of a class of chemical ingredients, the extracts obtained by extraction procedures underwent several chemical tests.

Presence of Alkaloid test: Dissolve 0.5 gm of extract in 10ml of dilute hydrochloric acid, filtered the residue. The filtrate was applied for the test as presence of alkaloids.

A. Mayer's reagent test:

The filtrates were mixed with some amount of Mayer's reagent. A yellow cream colored precipitate was formed. This showed positive result or presence of alkaloids.

Preparation of Mayer's reagent: Take equal amount of 1.36 gm of mercuric chloride and dissolved in 60 ml of distilled water to prepare solution number A. The solution B was prepared by dissolving 5 mg of potassium iodide in 20 ml of distilled water. Both a and b solution was mixed in other test tube and adjust the volume was adjusted to 100 ml with distilled water.

B. Dragendorff's reagent Test: The filtrate were taken in test tube and treated with Dragendorff's reagent. The reddish brown colored precipitate was present and this showed positive result or presence of alkaloids.

Preparation of Dragendroff's reagent: Prepare solution A in one test tube by dissolving 8 gm of bismuth nitrate in 20 ml of nitric acid. The solution B was prepared by dissolving 27.2 gm of potassium iodide in 50 ml distilled water. Mixed both (a) and (b) solution in other test tube and adjust the volume was adjusted to 100 ml with distilled water.

C. Wagner's reagent test: The filtrate were taken in test tube and treated with Wagner's reagent. The reddish brown colored precipitate was present and this showed positive result or presence of alkaloids.

Preparation of Wagner's reagent: The solution of Iodine in Potassium Iodide was prepared in distilled water.

D. Hager's reagent Test: The filtrate were taken in test tube and treated with Hager's reagent. The yellow colored precipitate was present and this showed positive result or presence of alkaloids.

Preparation of Hager's reagent: The saturated solution of Picric acid was prepared in distilled water as Hager's reagent.

Presence of carbohydrates test:

A. Molisch's reagent test:

One milliliter of the filtrate was placed in a test tube and given a few drops of Molisch's reagent treatment. A 2 milliliter conc. H_2SO_4 was gently applied along the test tube's walls until a purple to violet hue ring formed at the intersection where the filtrate was present. The presence of carbohydrates in the plant extract was shown by the creation of a purple to violet colored ring at the intersection of the filtrate present.

Preparation of Molisch's reagent: Take 10 gm of α- napthol in beaker and dissolve by adding 100 ml of 95% alcohol till to prepare solution.

B. Fehling's reagent Test: The filtrate 1 ml of extract solution was mixed with 5 ml or equal volume of fehling's reagent A and B. The solution was boiled. The presence of brick red color ppt was showed positive result or presence of reducing sugar.

Preparation of Fehling's reagent:

Fehling's A: The saturated solution of Copper sulphate in distilled water.

Fehling's B: The saturated solution of Potassium tartarate and Sodium hydroxide in distilled water.

C. Barfoed reagent test: The most common method for identifying monosaccharide and polysaccharide sugars is the Barfoed reagent test.

Heat the test tube in a boiling water bath after taking 1 ml of the filtrate and mixing it with 1 ml of reagent. Within two minutes, the appearance of brick red precipitate indicated a good result for monosaccharide polysaccharides. After a lengthy heating period of around 10 minutes, the appearance of brick-red precipitate indicated a favorable outcome for disaccharide polysaccharides, which may lead to reduction by partial hydrolysis to monosaccharide.

D. Benedict reagent test: The filtrate 1 ml were taken in test tube and treated with few drops of Benedict's reagent and boil on water bath. During boiling, the presence of reddish brown precipitate showed positive result or presence of reducing sugars.

Preparation of Benedict reagent: The saturated alkaline solution of cupric citrate complex.

Presence of Glycoside tests:

A. Modified Borntrager's reagent test: One milliliter of the filtrate was placed in a test tube and given a few drops of ferric chloride solution. For five minutes, the solution was boiled in a bath of boiling water. After cooling, the solution mixes were shaken to add an equivalent amount of benzene. A separating funnel in another test tube was used to separate the benzene layer. Half the amount of the ammonia solution was applied to this divided layer containing test tube, and it was violently mixed. Anthraquinones gycosides were present in the ammoniacal layer when the color became rose pink or cherry red.

B. Keller killiani's reagent test: One milliliter of the filtrate was placed in a test tube and agitated or treated with one milliliter of glacial acetic acid solution. Prior to testing, a little quantity of ferric chloride material was added to the glacial acetic acid solution. Conc. The test tube's side wall was used to delicately add around 1 milliliter of sulfuric acid. The acetic acid layer exhibits blue coloration, whereas the presence of red color at the interface between the two liquids indicates the presence of glycosides or a favorable outcome.

C. Legal's reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with sodium nitropruside in pyridine and methanolic alkali. The presence of pink colour showed positive result or presence of cardiac glycosides.

D. Baljet reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with few drops of sodium picrate reagent. The presence of yellowish orange colour showed positive result or presence of cardiac glycosides.

Presence of phytosterols and Triterpenoids test:

A. Liebermann reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with 1 ml of acetic anhydride solution. The solution were heated on a boiling water bath for 5 min and cooled. After cooling solution were mixed with few drops of conc H_2SO_4 by the side wall of the test tube. The presence of blue color showed positive result or presence of sterols.

B. Libermann-Burchard reagent test: One gram of extract was placed in a test tube, agitated, and treated with two milliliters of chloroform before being filtered. When the collected filtrate was boiling on a water bath, a few drops of acetic anhydride solution were added. The solution mentioned above was cooled to room temperature. A few drops of concentrated H2SO4 were combined by the test tube's side wall once the solution had cooled to the ideal temperature. A brown ring was seen where two layers joined, and the top layer became green, indicating the presence of sterols. The creation of a deep red hue indicated the presence of triterpenoids.

C. Salkowaski reagent test: The extract 1 gm were taken in test tube and treated or shaken with chloroform and few drops of concentrated Sulphuric acid. Allow the solution to stand for some time and, presence of red color appears in the lower layer showed positive result or presence of sterols and formation of yellow colored at lower part showed positive result or presence of triterpenoids.

Presence of Protein and Amino acids test: Dissolve 100 mg of extract in 10 ml of water, filtered the residue. The filtrate was applied for the test as presence of protein and amino acids.

A. Millon's reagent test:

The filtrate 2 ml were taken in test tube and treated or shaken with 2 ml of Millon's reagent. The solution was boiled in a water bath for 5 minutes, cooled at optimum temperature. The solution was mixed with few drops of $NaNo_2$ solution. The white precipitate was observed and it was boiled, which turns to red in color showed positive result or presence of proteins and amino acids.

Preparation of Millon's reagent: Take 1 gm mercury with 9 ml of fuming nitric acid in test tube and keeping the mixture in cooled environment during the reaction. As the reaction was completed add equal volume of distilled water in above solution.

B. Ninhydrin reagent test:

The filtrate of extract upto 2 ml were taken in test tube and treated or shaken with, 0.25% Ninhydrine reagent and boiled for 2 minutes. The presence of blue colour showed positive result or presence of amino acids.

Preparation of Ninhydrin's reagent: Prepare 0.25% solution of ninhydrin in n-butanol as solvent.

C. Biuret reagent test: The filtrate 2 ml were taken in test tube and treated or shaken with 2 ml of 10% sodium hydroxide and heated for 10 minutes. A drop of 7% copper sulphate was added in the above mixture. The presence of purplish violet colour showed positive result or presence of proteins.

Presence of Phenolic and Tannins test:

A. Ferric chloride reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with 2 ml of 1% ferric chloride solution. The presence of greenish- black colour showed positive result or presence of phenolic nucleus.

B. Lead Acetate reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with few drops lead acetate solution. The presence of yellow precipitate showed positive result or presence of tannins.

C. Alkaline reagent test: The filtrate 1 ml were taken in test tube and treated or shaken with sodium hydroxide solution. The presence of **yellow** to **red** precipitate within short time showed positive result or presence of alkaline materials.

Presence of Flavonoids test:

A. Shinoda reagent test (Magnesium Hydrochloride reduction test): Take 100 mg of extract in test tube and treated or shaken with few fragments of magnesium metal. The concentrated hydrochloric acid was added drop wise. The presence of magenta colour showed positive result or presence of Flavanoids.

C. Alkaline reagent Test: The filtrate 1 ml were taken in test tube and treated or shaken with few drops of Sodium hydroxide solution. The presence of an intense yellow color which turns to colorless on addition of few drops of dilute acetic acid showed positive result or presence of flavonoids.

Presence of Oils and Fats test:

A. Oily spot test: The filtrate one drop was placed on filter paper and solvent was allowed to evaporate. An oily stain on filter paper showed positive result or presence of fixed oil.

Presence of Saponins test:

A. Foam Test: One milliliter of the filtrate was placed in a test tube and shaken or treated with distilled water for fifteen minutes. The presence of saponins or sustained foam indicated a favorable outcome. Sugars, glycosides, tannins, phenolic compounds, gums, and mucilage were all found in the ethanolic extract, but no saponins, alkaloids, phytosterols, fixed oils, lipids, proteins, amino acids, or volatile oils were.

In-vivo pharmacological screening (Anti-depresant activity)

Drugs and Chemicals: Sourced from Sigma Company USA, Merck Germany, Sisco Research Laboratory, Mumbai, Qualigens Mumbai, Across Organics Mumbai, Spectrochem, Mumbai, or S.D. Fine chemicals Mumbai, all the chemicals used in these experiments were of the highest quality. Every organic solvent that was used was AR grade. Biological sample preparation and estimate were carried out using spectroflurometer (Elico model), spectrophotometer (Schimatzu model UV 1601) double beam, chilled super speed centrifuge (Sorvall RC-5B model), and light microscope (Lynx, Lawrence and Mayo).

Animals utilized in the experiments: Male mice weighing between 100 and 125 grams were used. Under typical laboratory circumstances, these mice had access to water and food. The National Institute of Nutrition, India's requirements for the care of the animals used in this research were followed, and the Institutional Animal Ethics Committee gave its approval (IAEC). Between one and three p.m., experiments were conducted by an observer who was not aware of the nature of each treatment. Different extract dosages were individually suspended in a vehicle containing 1% (w/v) tween 20 in distilled water for the behavioral test. The usual medication, amitriptyline and fluoxetine, was administered by gastric gavage once daily for 1, 3, 7, 14, and 21 days. An hour after the most recent dose or therapy, a behavioral test was performed.

A. Forced swimming test (FST): Animal groups: A total of 48 mice were used for the activity. We were split up into six groups at random, with eight mice in each group. The mice in each group received the care indicated in the table and were handled as follows: Group 2 serves as the experimental control (FST group) while Group 1 serves as the usual control. Group 2 also has tween-20 suspensions. Oral administration of three distinct dosages of Rhodiola rosea ethanol extract was given to groups 3-5. Groups 3 and 4 were given 100 mg and 200 mg of extract/kg and 300 mg of extract/kg of body weight, respectively. Group 5 received no treatment at all. The rats in Groups 6 and 7 were given amitriptyline and fluoxetine (10 mg/kg body weight), which are common antidepressants.

Design of the experiment: The FST was carried out on mice, with the exception of group 1, where each group was tested by swimming in a cylindrical glass tank with a diameter of 50 by 30 cm and water at a temperature of 25±2ºC. The mice were given six minutes to swim, and a video monitoring device was used to determine the amount of time the mice remained immobile during the test's last four minutes. The mouse was said to be immobile during this stage if it was only making the motions required to maintain its head above water while floating motionless in the water. After swimming sessions, they were dried with towels. The effects of oral treatments with LIEOH for 1, 3, 7, 14, and 21 consecutive days were studied to ascertain the time-dependent effects on immobility time 39–40.

Table 1: Experiment animal groups (FST)

Animal groups	Treatment
Group 1	Normal control
Group 2	Tween-20 suspensions + FST
Group 3	LIEOH (100 mg/kg b wt.) + FST
Group 4	LIEOH (200 mg/kg b wt.) + FST
Group 5	LIEOH (300 mg/kg b wt.) + FST
Group 6	Amitriptyline (10 mg/kg b wt.) + FST
Group 7	Fluoxetine (10 mg/kg b wt.) + FST

B. Tail suspension test (TST):

Animal groups: A total of 48 mice were used for the activity. We were split up into six groups at random, with eight mice in each group. The mice in each group received the care indicated in the table and were handled as follows: Group 1 act as normal control and Group 2 have tween-20 suspensions and act as experimental control (TST group). Oral administration of three distinct dosages of Rhodiola rosea ethanol extract was given to groups 3-5. Groups 3 and 4 were given 100 mg and 200 mg of extract/kg and 300 mg of extract/kg of body weight, respectively. Group 5 received no treatment at all. The rats in Groups 6 and 7 were given amitriptyline and fluoxetine (10 mg/kg body weight), which are common antidepressants.

Table 2: Experiment animal groups (TST)

Animal groups	Treatment
Group 1	Normal control
Group 2	Tween-20 suspensions + TST
Group 3	LIEOH (75mg/kg b wt.) + TST
Group 4	LIEOH (150mg/kg b wt.) + TST
Group 5	LIEOH (300mg/kg b wt.) + FST
Group 6	Amitriptyline (10mg/kg b wt.) + TST
Group 7	Fluoxetine (10mg/kg b wt.) + TST

Experiment design: To test tail suspension, a box with 35 cm on each wall side was employed. The apparatus's front surface was exposed, and each mouse was hung by attaching its tail to the center of the top surface using a tail hanger and non-irritating adhesive tape, with its head positioned five centimeters below the surface. For five minutes, the experiment was conducted in a dimly lit room with little background noise. In the last four-minute interval of the test, the whole length of immobility (total immobility time) was observed and quantified. A video camera mounted just above the box captured every test session. Only when mice hung still and passively were they deemed immobile [41–42].

C. Elevated plus maze test: The most widely used and authorised technique for measuring anxiety in animal models is the elevated plus maze test (EPMT). The mechanical assembly had four arms, two of which were closed and the other two of which were left open. At an interior position (5 cm2 x 5 cm2), open arms (35 cm2 x 5 cm2) were crossed with closed arms (35 cm3 x 5 cm3 x 20 cm3). The behavioral tests were conducted in a room with reduced noise levels and low light. The animals were divided into several treatment groups, and after a half-hour, they were placed only on the EPM device in the center, facing one of the closed arms. The time each animal spent with its arms open and closed was recorded for 300 seconds (give or take a few seconds). The number of open arm entries (OAE) and behavioral assessments of the amount of time spent on the middle platform or in the open and closed arms (expressed as a percentage of the total test time) were used to evaluate the anxiolytic-like effects. When a mouse inserted all four paws into an arm, that entry was scored. The amount of head dips (DIPs, or exploratory movements of the head and shoulders over the maze's sides) and stretch-attend postures (SAPs, or exploratory postures in which the mouse extends forward and retracts to its initial position without moving forward) were the other metrics examined.

Results and Discussion

Collection and authentication of plant material: The selected plant material Rhodiola rosea roots were collected from local area of Indore, (M. P.) India, and authenticated by botanist.

Prelimnary phytochemical analysis of extracts: After being extracted (ethanol extract) from a chosen plant, Rhodiola rosearoots drugs, using the soxhlet method, the plant's secondary metabolites (alkaloids, glycosides, tannins, flavonoids, sterols, fats, oils, phenols, and saponins) were determined by qualitative phytochemical tests. Sugars, glycosides, tannins, phenolic compounds, gums, and mucilage were all found in the ethanolic extract, but no saponins, alkaloids, phytosterols, fixed oils, lipids, proteins, amino acids, or volatile oils were. The findings are shown in the table.

Table 3: Phytochemical analysis of *Rhodiola rosea roots* extracts

S. No.	Phytochemical	Indication test	Ethanol extract
1	Alkaloid	Dragendorff test	-
2	Napthoquinon	Juglone test	+
2	Steroid	Salkowaski test	-
3	Carbohydrates	Molish test	+
4	Triterpene	Vanillin-sulphuric acid test	-
5	Tannin	Ferric chloride test	+
6	Glycosides	Keller-killani test	+
7	Protein	Biuret test	-
8	Flavonoid	Shinoda Test	+
9	Saponin	Lead acetate test	-
10	fixed oils, fats		-

Where + is Present and – is Absent

In-vivo antidepressant activity (Anti-depressant activity):

Effect of LOET, amitriptyline and fluoxetine pre-treatment on body weight mice (FST and TST groups): Table displays the impact of extract on the change in body weight. The findings indicated that there was no variation in the animals' body weight growth across all treatment groups, whether they had a one-day, three-day, or seven-day regimen. After taking the medication orally for seven days, two to three weeks, or fourteen to twenty-one days, there was a little rise in weight gain. Mice's weight growth might be equivalent to rats' typical weight rise. It has been shown that giving animals LIEOH has no impact on their weight.

Table 4: Effect of LOET, amitriptyline and fluoxetine pre-treatment on body weight in mice (FST groups)

Days	Body weight (g) during different treatment period						
	Groups						
	Group 1	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**	**Group 7**
1	107.8±2.1	106.6±1.5	109.2±2.1	110.5±2.1	108.5±3.6	106.4±1.4	104.3±1.4
3	108.4±1.2	108.8±1.7	111.6±2.5	116.2±1.1	110.5±2.6	107.9±2.1	106.1±1.6
7	110.6±21	111.4±3.2	113.4±3.4	117.4±2.4	111.4±3.8	110.2±2.1	107.5±1.6
14	111.5±1.9	115.4±2.1	116.1±3.3	119.5±3.6	113.3±3.3	111.7±2.1	109.7±2.2
21	114.3±2.1	118.9±2.3	122.8±1.9	121.4±2.1	113.8±2.1	112.8±1.3	112.4±1.2

Values are presented as the mean ± SD (n=8). There were no significant differences at $p<0.05$.

Table 5: Effect of LOET, amitriptyline and fluoxetine pre-treatment on body weight in mice (TST groups)

	Body weight (g) during different treatment period						
	Groups						
Days	**Group 1**	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**Group 6**	**Group 7**
1	102.1±2.2	102.1±11	103.1±1.3	106.1±1.1	103.1±1.6	100.1±1.1	100.3±1.1
3	105.7±1.7	103.8±1.1	105.4±1.2	107.1±2.1	104.2±1.1	100.7±1.5	101.2±1.3
7	108.6±11	105.1±2.2	106.3±1.4	109.1±1.4	105.1±1.3	101.1±1.7	102.1±1.1
14	111.1±1.2	107.3±2.1	106.9±2.3	110.2±2.1	108.7±1.2	102.2±2.2	103.2±1.1
21	115.5±2.3	109.2±1.1	107.2±2.1	112.1±1.1	109.2±1.8	103.2±2.1	104.1±1.1

Values are presented as the mean ± SD (n=8). There were no significant differences at $p<0.05$.

Effect of LOET, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (FST and TST groups): Mice used in FST are made to swim in a confined area from which they are unable to escape, leading to the typical behavior of immobility. Several substances that are therapeutically successful in treating depression in humans diminish this behavior, which is indicative of a sense of hopelessness. Similar to the FST, the TST also causes animals to experience hopelessness. This immobility was examined by potential time-dependent effects on immobility time. This immobility is known as behavioral despair in animals and is acknowledged as a condition akin to human depression. The standardized application schedule, which was preceded by the appropriate vehicle control application, was used to examine the oral treatments with LOET for 1, 3, 7, 14, and 21 consecutive days, respectively. The animals' antidepressant-like performance in the FST is shown by a decrease in the length of time they remain immobile. In a dose-dependent way, LIEOH treatment significantly reduced the immobility period in mice during forced swimming tests at doses of 100, 200, and 300 mg/kg. Table and Figure FST and Table and Figure TST, respectively, show the effects of LOET, amitriptyline, and fluoxetine on immobility in mice. In mice in FST and TST, the clinical antidepressant effects often manifest after long-term therapy. The findings revealed that there was a little reduction in immobility time after the third and seventh days of therapy; this reduction was not statistically significant at $p<0.05$. After receiving LOET pretreatment for 14 and 21 days, the mice were able to swim. The traditional antidepressants amitriptyline and fluoxetine had the same impact, as did stress management, in terms of reducing the length of immobility. After receiving oral therapy for 14 days, LOET at 300 mg/kg body weight showed a substantial reduction in the length of immobility. Following a 21-day LOET therapy, the dosage in

immobility time showed a substantial therapeutic impact. The highest reported impact was 300 mg/kg b.wt., which resulted in a decrease in immobility time when compared to antidepressant medications like as fluoxetine and amitriptyline.

Table 6: Effect of LOET, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (FST groups)

Group	Dose mg/ kg b.wt	Duration of immobility (s)				
		Days				
		1	3	7	14	21
Group 1	Normal control	-	-	-	-	-
Group 2	Tween-20 suspensions + FST	112.1±7.1	102.1±3.1	108.1±6.3	103.4±5.1	105.4±3.9
Group 3	LOET (100 mg/kg b wt.) + FST	103.4±6.6	87.1±4.1^{a}	89.1±3.6	75.4± 4.1^{a}	66.2±3.6^{a}
Group 4	LOET (200 mg/kg b wt.) + FST	98.2±8.3	84.5±3.3^{a}	76.2±4.3^{a}	59.7±5.1^{a}	57.4±5.7^{a}
Group 5	LOET (300 mg/kg b wt.) + FST	89.3±86.1^{a}	76.1±4.1^{b}	66.1±4.7^{b}	41.8±2.1^{b}	24.2±4.6^{b}
Group 6	Amitriptyline (10mg/kg b wt.) + FST	73.1±7.2^{b}	66.3±6.1^{c}	56.2±5.1^{c}	29.2±5.4^{b}	15.4±2.9^{c}
Group 7	Fluoxetine (10mg/kg b wt.) + FST	79.4±9.2^{a}	69.6±3.1^{b}	67.1±3.1^{b}	36.0±4.6^{c}	22.5±2.2^{b}

Values are presented as the mean ± SD (n=8). Values bearing different superscripts in the same column are significantly different ($p<0.05$) (ANOVA).

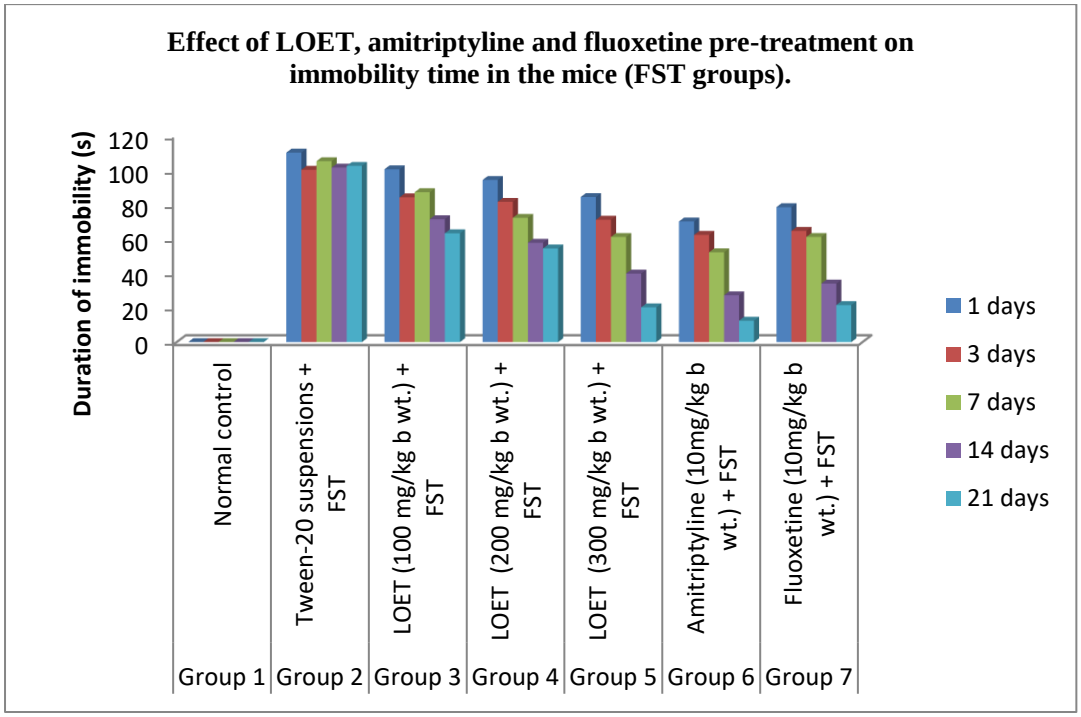

Figure 2: Effect of LOET, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (FST groups)

Table 7: Effect of LOET, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (TST groups)

Group	Dose mg/ kg b.wt	Duration of immobility (s)				
		Days				
		1	3	7	14	21
Group 1	Normal control					
Group 2	Tween-20 suspensions + TST	93.3±3.9	92.7±6.1	93.4±4.3	91.4±3.7	89.1±5.7
Group 3	LOET (100 mg/kg b wt.) + TST	87.5±3.6	85.6±6.8[a]	84.4±4.3	78.7±4.7[a]	75.2±1.7[a]
Group 4	LOET (200 mg/kg b wt.) + TST	86.1±3.1	77.8±6.6[a]	73.7±3.2	74.6±3.6[a]	69.6±2.2[a]
Group 5	LOET (300 mg/kg b wt.) + FST	86.6±3.4	71.4±5.1[b]	66.1±4.4[a]	65.8± 4.7[b]	60.2± 3.7[b]
Group 6	Amitriptyline (10mg/kg b wt.) + TST	79.5±3.1	67.7±6.4[b]	59.7±3.1[a]	56.4±3.4[b]	51.4±2.4[b]
Group 7	Fluoxetine (10mg/kg b wt.) + TST	74.8±3.6	67.0±4.6[b]	55.4±4.6[a]	49.5±3.7[b]	46.5±4.1[b]

Values are presented as the mean ± SD (n=8). Values bearing different superscripts in the same column are significantly different ($p<0.05$) (ANOVA).

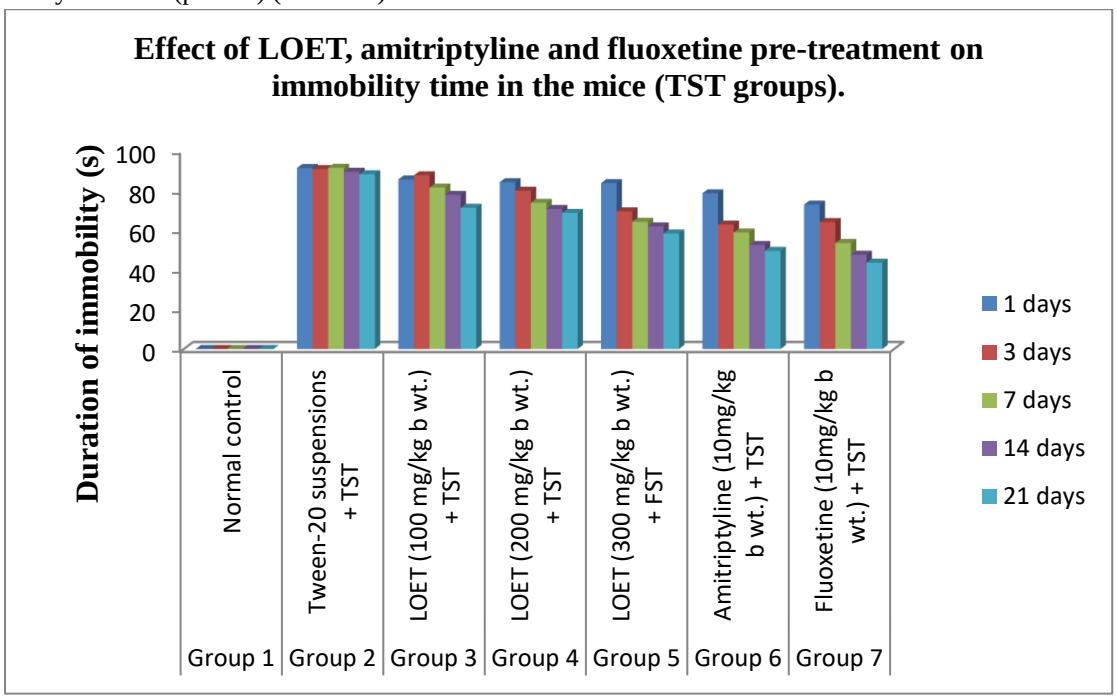

Figure 3: Effect of LOET, amitriptyline and fluoxetine pre-treatment on immobility time in the mice (TST groups)

Elevated plus maze test: The most widely used and authorised technique for measuring anxiety in animal models is the elevated plus maze test (EPMT). The number of open arm entries (OAE) and behavioral assessments of the amount of time spent on the middle platform or in the open and closed arms (expressed as a percentage of the total test time) were used to evaluate the anxiolytic-like effects. When a mouse inserted all four paws into an arm, that entry was scored. The amount of head dips (DIPs, or exploratory movements of the head and shoulders over the maze's sides) and stretch-attend postures (SAPs, or exploratory postures in which the mouse extends forward and retracts to its initial position without moving forward) were the additional factors that were examined. The traditional antidepressants amitriptyline and fluoxetine had the same impact, as did stress management, in terms of reducing the length of immobility. Following oral administration for 14 days, there was a substantial reduction in the duration of immobility with LIEOH at 300 mg/kg body weight.

Table 8: Effect of LOET, on time spent in open arms and time spent in closed arms in elevated plus maze model

Group	Dose mg/ kg b.wt	Time Spent in Open Arms (s)	Time Spent in Closed Arms (s)
Group 1	Normal control	32.15±3.05	216.17±3.11
Group 2	Tween-20 suspensions + TST	101±7.92	189.04±4.19
Group 3	LOET (100 mg/kg b wt.) + TST	51.02±4.12	241.21±2.14
Group 4	LOET (200 mg/kg b wt.) + TST	71.02±5.02	210.11±3.84
Group 5	LOET (300 mg/kg b wt.) + FST	93.04±6.02	207.14±4.24

Values are presented as the mean ± SD (n=8). Values bearing different superscripts in the same column are significantly different ($p<0.05$) (ANOVA).

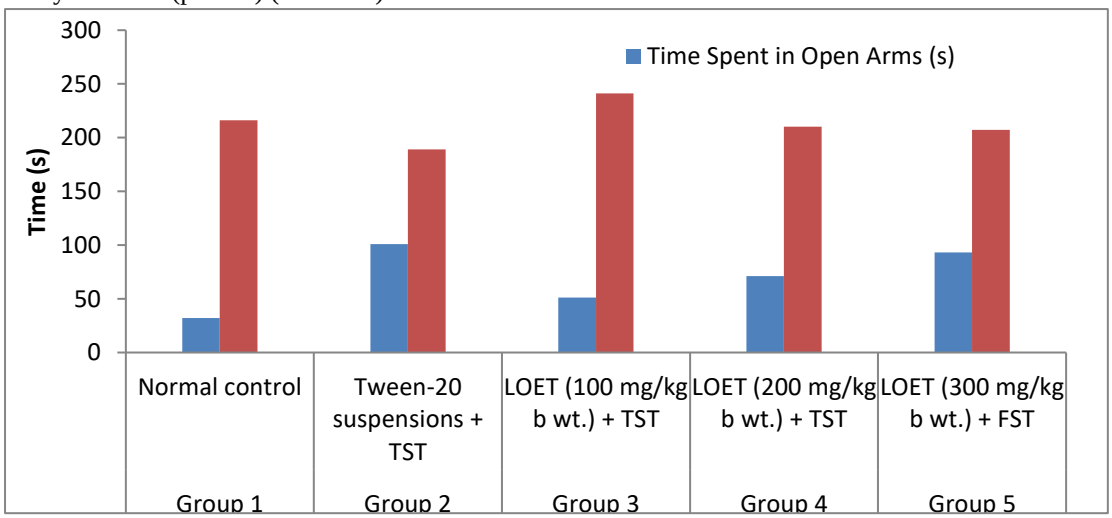

Figure 4: Effect of LOET on time spent in open and closed arms in the mice (Elevated plus maze)

Summary and Conclusion

In addition to its biological roots, mental sadness also has emotional components. Symptoms of depression include apathy, pessimism, uncertainty, poor self-esteem (characterized by feelings of guilt, inadequacy, and ugly), indecision, and motivation loss. Major depressive disorder patients have symptoms that are indicative of abnormalities in brain monoamine neurotransmitters, including dopamine, serotonin, and adrenaline. Moreover, there may be other drug-drug interactions. These circumstances give rise to the possibility of using medicinal plants

as an alternate form of therapy for depression. Our goal is to investigate the potential of medicinal plants in the management of depression, as all synthetic medications now available for the treatment of depression have a variety of negative effects linked to hazardous interactions. The current research is suggested the existence of additional phytochemical elements in rhodiola rosea roots gives them a more effective action for managing depression, which justifies the suggested effort. The application of MeOH to Rhodiola rosea roots at effective doses ranging from 150 mg to 300 mg resulted in a noteworthy impact on the immobility period of all animals in various groups. The highest reported impact was 300 mg/kg b.wt. permitted a decrease in the amount of time spent immobile in comparison to antidepressants like amitriptyline and fluoxetine. Thus, it was determined that the ethanolic extract of Rhodiola rosea roots, at an effective dose supported by the current investigation, could cure depression caused in mice and humans alike.

References

[1]. Galderisi S, Heinz A, Kastrup M, Beezhold J, Sartorius N, (2015) Toward a new definition of mental health." World psychiatry, *Official journal of the world psychiatric association* (WPA), 14, 2, 231–233.

[2]. Patel V, Kleinman A. (2003) Poverty and common mental disorders in developing countries. *Bulletin of the World Health Organization*, 81, 609-615.

[3]. Taube-Schiff M, Lau MA. (2008) In Major depressive disorder. Hersen, M.– Rosqvist, J.(szerk.) Handbook of psychological assessment, case conceptualization, and treatment, 1, 319-351.

[4]. Addis ME, Jacobson NS, (1996) Reasons for depression and the process and outcome of cognitive–behavioral psychotherapies. *Journal of consulting and clinical psychology*, 64, 6, 1417.

[5]. McKeon P, Carrick S. (1991) Public attitudes to depression: A national survey. *Irish Journal Of Psychological Medicine*. 8, 2, 116-121.

[6]. Matschinger H, Angermeyer MC. (1996) Lay beliefs about the causes of mental disorders: a new methodological approach. *Social psychiatry and psychiatric epidemiology*, 31, 6, 309-315.

[7]. Jorm AF, (1990) Mental health literacy: Public knowledge and beliefs about mental disorders. *The British Journal of Psychiatry*, 177, 5, 396-401.

[8]. Jorm AF, Korten AE, Jacomb PA, Christensen H, Rodgers B, Pollitt P, (1997) Public beliefs about causes and risk factors for depression and schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, 32, 3, 143-148.

[9]. Razali SM, Khan UA, Hasanah CI, (1996) Belief in supernatural causes of mental illness among Malay patients: impact on treatment. *Acta psychiatrica scandinavica*, 94, 4, 229-233.

[10]. Angermeyer MC, Matschinger H, Riedel-Heller SG, (1999) Whom to ask for help in case of a mental disorder? Preferences of the lay public. *Social psychiatry and psychiatric epidemiology*, 34, 4, 202-210.

[11]. American Psychiatrie Association. *Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.*

[12]. Angst J, (1997) Depression and anxiety: implications for nosology, course, and treatment, *J Clin Psychiatry*. 58, 8, 3-5.

[13]. Kendler KS, Thornton LM, Prescott CA, (2001) Gender differences in the rates of exposure to stressful life events and sensitivity to their depressogenic effects, *Am J Psychiatry*, 158, 4, 587-93.

[14]. Kendler KS, Gardner CO, Neale MC, Prescott CA, (2001) Genetic risk factors for major depression in men and women: similar or different heritabilities and same or partly distinct genes? *Psychol Med*. 31, 4, 605-16.

[15]. Kandel ER, Squire LR, (2000) Neuroscience: breaking down scientific barriers to the study of brain and mind, *Science*. 290, 549, 1113-20.