

# Thymol as a Potent Anti-Schizophrenic Agent in Swiss Albino Mice

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#### **Abstract**

In ancient medical systems, the plant Thymus vulgaris L. was used widely for various medicinal purposes. The leaf portion of Thymus vulgaris L. along with its isolated active phytoconstituent thymol was studied in the management of anti-schizophrenic activity in Swiss albino mice. The present work deals with the *in vivo* antischizophrenic activity study of thymol by inhibition of apomorphine climbing mice and methamphetamine-induced stereotypical behaviour in mice models. Thymol was isolated from Thymus vulgaris L leaves and confirmed by TLC and FTIR spectroscopy. Experimental works included Actophotometer, mice treated with Thymus vulgaris leaves extract TVLE (50mg/kg and 100mg/kg) and its bioactive moiety thymol (5mg/kg) along with aripiprazole (1mg/kg). Investigations of the anti-schizophrenic activity of TVLE (50mg/kg and 100mg/kg) and thymol (5mg/kg) showed a significant (\*\*p<0.01) results in both models of methamphetamine-induced stereotypy and apomorphine climbing time in experimental mice. Based on the experimental findings TVLE and thymol were shown to be very much effective as anti-schizophrenic activity. The results explained the role of thymol acting like a dopaminergic blocker or by causing a decrease in the brain's dopamine supply to improve the schizophrenic-like behaviour in Swiss albino mice.

Keywords: Anti-Schizophrenic Activity, Aripiprazole, Dopaminergic Antagonist, Neurotoxin Thymol

#### 1. Introduction

Medicinal plants are utilized as supplementary or alternative therapies all over the world. Studies on these medicinal plants that take into account pharmacological and toxicological evaluations are essential for the creation of novel medications. The different plant parts along with the whole plant are used to make herbal treatments. They are absorbed either orally, topically, or via inhalation<sup>1</sup>. Traditional medical systems like Unani, Ayurveda, and Chinese medicine frequently employed medicinal treatments native people in Rome, Egypt, Iran, Africa, and America used plants in healing rituals. Folk medicinal methods are still widely used in many areas. One of the world's oldest civilizations, India is known for having one of the largest plant collections. A vast diversity of aromatic and medicinal plants, which are mainly gathered as basic materials for the production of pharmaceuticals and fragrance items,

are primarily found in India's forests. Approximately 8,000 herbal remedies have been prescribed in Indian medical traditions. Folk (tribe) therapies are the four basic indigenous medical techniques<sup>2</sup>.

Schizophrenia is characterised by various symptoms such as hallucinations, illusions, incomprehensible speech or actions, and impaired intellectual functioning. Dopaminergic signalling disruption has been implicated as the cause of these symptoms<sup>3,4</sup>. Typically, schizophrenia first appears in late adolescence or early adulthood. However, it can appear during the Middle Ages<sup>5</sup>. It has been found to affect men far more severely and frequently than it does women. Schizophrenia has a significant human cost, but it is also associated with higher rates of disease and mortality.

Keeping in mind all this background the current research work was aimed to perform the antischizophrenic activity of thymol by inhibition of apomorphine climbing time and methamphetamine

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(METH) induced stereotypical behaviour in Swiss albino mice.

#### 2. Material and Methods

#### 2.1 Plant Procurement and Authentication

The *Thymus vulgaris* (leaves) were collected from Prakriti Garden Studio, Chattarpur, New Delhi in Jan 2022. It was authenticated from the Botanical Garden of the Indian Republic, Sector-37, Noida, Delhi in February 2022. A voucher specimen was saved in the Botanical Garden of the Indian Republic (No. BSI\BGIR/1/TECH/2021/047, dated 8.2.2022).

#### 2.2 Extraction of Plant Materials

The dried leaves (100g) of *Thymus vulgaris* were extracted with ethanol (500ml) using the Soxhlet apparatus. The liquid extract was filtered, air-dried and then kept in a hot water bath to get a more solid extract. Then the ethanol extract was concentrated and weighed. The dry extract was stored at 4°C until used (Figure 1).

The percentage yield was then calculated by following the formula:

$$% yield = \frac{\text{Weight - empty China dish}}{\text{Weight of powder drug}}$$

#### 2.3 Isolation of Thymol

Ethanol solvent was used in the isolation of thymol from *Thymus vulgaris* leaves. Using a Soxhlet extractor



**Figure 1.** Extraction of *Thymus vulgaris* L. by Soxhlet apparatus.

and 7500 ml (95%) ethanol, 500g of powdered *Thymus vulgaris* leaves was extracted for 16-18 hrs. After screening, the extract was boiled to 60°C in a water bath to concentrate it. The filtrate was collected and add 10 ml of a 10% potassium hydroxide solution, which was then constantly stirred. After removing the remaining insoluble material, the alcohol extract was allowed to stay overnight before being filtered using a membrane filter.

### 2.4 Isolation of Thymol by TLC Procedures

The glass plates  $(20 \times 20 \text{ cm})$  were covered with silica gel  $G_{60}$  for a TLC thickness of 0.25mm. Thymol essential oil was dissolved in methylene chloride, along with a standard of thymol and extracts produced by soxhlet extraction using methylene chloride, TVLE. Benzol: Ethyl acetate was the mobile phase (93:7; V/V). The plate was sprayed with 1% vanillin solution to identify and then heated (shortly at  $105^{\circ}\text{C})^{6}$ .

#### 2.5 Experimental Animal

Swiss albino mice of around 25-30 gm of male gender were used in this experiment. They were obtained from Central Animal House from the Noida Institute of Engineering and Technology (Pharmacy Institute), Knowledge Park II, in Greater Noida (CPCSEA/ IAEC/NIET/2022/01/03). It was acquired from the Institutional Animal Ethics Committee (IAEC) of the NIET (Pharmacy Institute) in Greater Noida, India. Water was supplied to the mice ad libitum, and they were kept in a 22°C room with a temperature and moisture content of 50-70 %. An authorised vendor of the supplied animals' food, UP State Agro Industrial Corporation Ltd. Lucknow, Uttar Pradesh. This investigation provides a guarantee that all experiments on animals were completely safe and performed as per CPCSEA guidelines.

### 2.6 Gross Behavioural Activity

In the gross behavioural study, male Swiss albino mice, weighing 20–25 gm, and 90 days old were used. Six animals comprised into five groups (n = 6). The first group served as control. The second group was standard Apomorphine 2.5mg/kg, with diazepam 5mg/kg given s.c. respectively. For the remaining Groups III, IV and V test groups, TVLE was given i.p. at concentrations of 50mg/kg, 100mg/kg and thymol (5mg/kg) along with

Aripiprazole (1mg/kg). Following the administration of test samples, the animals were continually monitored for the first four hrs for any observed behavioural changes and for death, at the end of 24 hrs, 48 hrs, and 72 hrs.

# 2.7 Locomotor Activity by using Actophotometer

Actophotometer was used to measure locomotor activity. For 10 minutes, each mouse was placed separately in the actophotometer to calculate their baseline activity scores<sup>7</sup>. The animals were then separated into 5 groups, each with 6 animals.

**Group I** - (Control Group) Animals were treated with Apomorphine (2.5mg/kg), s.c.

**Group II** - (Standard Group) Animals were treated with diazepam (5mg/kg) i.p. + Apomorphine 2.5mg/kg, s.c.

**Group III** - (Test Group-I) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (50mg/kg) i.p.

**Group IV** - (Test Group-II) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (100mg/kg) i.p.

**Group V** - (Test Group-III) Animals were treated with Aripiprazole (1mg/kg) i.p. +Thymol (5mg/kg) i.p.

### 2.8 Experimental Procedure

Using actophotometer, the potential TVLE and thymol were investigated. In this method, five groups (n=6) of six Swiss albino mice of either sex (weighing 25–30 g) were randomly separated. The activity of each animal in the first group was observed for 10 mins within the activity cage. The mice were then administered 2.5mg/kg (s.c.) of apomorphine, and their levels of activity were checked again 30 minutes later. The second, third and fourth groups of experimental mice were performed orally administrated with TVLE (50mg/kg and 100mg/kg) and thymol (5mg/kg), respectively. The following formula was used to determine the percentage of each animal's motor activity reduction:

% reduction in locomotor activity = (Wa - Wb/Wa) × 100 %

where, Wa and Wb are average activity scores before and after treatment, respectively.

### 3. Anti-Schizophrenia Activity

# 3.1 Inhibition of Apomorphine Climbing in Mice

Antipsychotic medication has been predicted using behavioural tests or animal models. These include the suppression of apomorphine and amphetamine-induced climbing in mice, the suppression of amphetamine-induced hyperactivity in mice, the suppression of conditioned avoidance responses in mice, and the suppression of apomorphine-induced loss of startle response in mice. By examining the response of antipsychotic medicines in diverse animal models of schizophrenia, one can obtain important insights into the mechanisms of action for these treatments since each animal model targets a different neurotransmitter system (dopaminergic neurotoxin)<sup>8</sup>.

Swiss albino mice with a body weight of about (25-30 gm) were divided into 5 groups and each group contain 6 animals:

**Group I** - (Control Group) Animals were treated with Apomorphine (2.5mg/kg) s.c.

**Group II** - (Standard Group) Animals were treated with Standard drug Risperidone (0.2mg/kg) i.p + Apomorphine (2.5mg/kg) s.c.

**Group III** - (Test Group-I) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (50mg/kg) i.p.

**Group IV** - (Test Group-II) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (100mg/kg) i.p.

 $\label{eq:Group-III} \textbf{Group-III)} \ \ \text{Animals were treated} \\ \text{with Aripiprazole (1mg/kg) i.p.} + \text{Thymol (5mg/kg) i.p.} \\$ 

### 3.2 Experimental Procedure

Apomorphine administration to mice caused them to participate in strange climbing behaviour that was initially characterized by rising and thereafter by spontaneous climbing activity. The mice were split into 5 groups, each with 6 mice. As a control, one group received merely a vehicle injection, while the other groups received active medication solutions at various concentrations. Before the studies, the animals were housed for an hour in a cylindrical wire mesh cage with dimensions of 13 cm in height, 14 cm in diameter, and 3 mm mesh. The apomorphine (2.5 mg/kg) subcutaneous

injection was given 20 minutes after the intraperitoneal administration of the antipsychotic medication. Beginning 10 minutes after apomorphine delivery, climbing behaviour was monitored for 20 minutes and assessed visually every 5 mins. The scoring scale was as follows: 0 for no paws on the cage, 1 for one, 2 for two, 3 for three, and 4 for four paws on the cage. Each score was recorded and based on the location of the paws at each inspection time point (within a 5-mins time frame). The animals' climbing behaviour was observed, and any other behavioural changes were recorded.

# 3.3 Methamphetamine (METH) Induced Stereotypical Behaviour in Mice

The relationship between methamphetamine-induced stereotypical behaviour in mice using, the antipsychotic type model is the dopaminergic system. Stereotypy and climbing behaviours were seen to be produced by the therapy after 7 and 21 days.

All animal groups of Swiss albino mice with a body weight of about (25-30 gm) were divided into 5 groups comprising 6 animals each:

**Group I** - (Control Group) Animals were treated with Methamphetamine (10mg/kg), i.p.

**Group II** - (Standard Group) Animals were treated with Risperidone (0.2mg/kg) i.p + Methamphetamine (10mg/kg) i.p.

**Group III** - (Test Group-I) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (50mg/kg) i.p.

**Group IV** - (Test Group-II) Animals were treated with Aripiprazole (1mg/kg) i.p. + TVLE (100mg/kg) i.p.

 $\label{eq:Group-III} \textbf{Group-III)} \ \ \text{Animals were treated} \\ \text{with Aripiprazole (1mg/kg) i.p + Thymol(5mg/kg) i.p.} \\$ 

### 3.4 Experimental Procedure

The cage's inner roof was placed over the animal, and the roof was then closed after 30 mins of administering methamphetamine. The methamphetamine-treated mice stayed on the cage's roof for longer than the saline-treated animal, which fell to the bottom more quickly since methamphetamine does not elicit spontaneous climbing activity. The cage's interior roof and wall were exposed for the full 30 mins of the measurement. For a period of 60 mins, the severity of each mouse's stereotyped behaviour was graded every 15 mins. Then, after giving the test medication TVLE and thymol to mice in various concentrations together with aripiprazole at

1mg/kg, i.p. was monitored every day for up to 35 days. The measures of sniffing, licking, repetitive movement, spinning, biting, circling, and head bobbing, compare to the control group receiving risperidone 0.2mg/kg intravenously with methamphetamine (10mg/kg i.p.).

Scores ranged from 0: no change from control to 1: periodic sniffing and constant exploration activity, 2: constant sniffing and periodic exploratory activity, 3: constant sniffing and periodic biting, chewing, or licking, and 4: constant sniffing and aperiodic exploratory activity, continuous sniffing, discontinuous biting and gnawing, or licking, continuous biting and gnawing or licking; no exploratory activity.

#### 4. Result and Discussion

#### 4.1 Estimation of Extracted Plant Material

The yield of TVLE and thymol obtained from leaves was found to be 10%w/w and 4.3%w/w on a dry weight basis.

### 4.2 Estimation of Isolated Compound

#### 4.2.1 Isolation of Thymol by TLC

The ethanol extract of leaves of Thymus vulgaris was diluted in 50ml of hot water and extracted three times with 50ml of ethyl ether and ethyl acetate respectively, to separate the components by TLC. The ethyl ether and ethyl acetate extracts were produced by using a rotary evaporator to separate solvents from each of the fractions examined. The TLC (normal-phase plates, ethyl ether-hexane, 1:5, v/v) separation of the ethyl ether extract allowed for the visualization of the nine zones on the TLC plate under UV light at 254 nm. After being scraped off the plate, ethanol was used to remove each zone. The active principles were determined using standardized criteria based on the R<sub>f</sub> values of the bands. After elution, the purity of each fraction was assessed using analytical TLC, which revealed a distinct separation of fractions. The isolated compound when viewed with UV light, indicated spots, and based on relative  $R_f$  values thymol was found to be at  $R_f$  0.52.

## 4.2.2 Spectral Characterization of Thymol by FTIR Spectroscopy

The compound isolated from the leaves of *Thymus* vulgaris was sent for its identity and purity check,

which was estimated quantitatively by FTIR spectra. By estimating its absorptions (bands) and matching with indicated functional groups, it was found to be a thymol. FTIR spectroscopy offers a quick and accurate method for estimating functional groups that exist in a molecule.

# 4.2.3 Phytochemicals Screening of Thymus vulgaris and Thymol

A wide range of phytochemicals are present in medicinal herbs, and they show various biological therapeutic activities. The extract of *Thymus vulgaris* and its bioactive moiety thymol were screened for preliminary phytochemical screening. The phytochemical testing was conducted by using different chemical tests with different solvents to identify the chemical nature of the phytoconstituents<sup>9</sup>. It was observed that TLVE and thymol revealed the presence of strong polar phytochemical compounds<sup>10</sup>.

It was seen from the given Table 1 that TVLE showed the presence of alkaloids, flavonoids, phenols, carbohydrates, and organic and inorganic compounds <sup>11</sup>. There is reported evidence that these phytochemicals have strong antipsychotic, antioxidant, antibacterial, antifungal, anti-inflammatory, antipyretic, and muscle relaxant as well evidence of cancer and hepatoprotective activities <sup>12</sup>.

### 4.3 Gross Behavioural Activity

# 4.3.1 Locomotors Activity by using Actophotometer

The locomotor activity of TVLE and thymol was determined with the use of an actophotometer. A reduction in locomotor activity has been observed (Table 2), which is a sign of drowsiness since it is used as a measure of alertness. Sedation and reduced locomotor activity are side effects of medications like benzodiazepines that have a sedative impact on the

**Table 1.** Preliminary qualitative phytochemical tests of TVLE and thymol

S.	Chemical Tests	TVLE (Thym	nus vulgaris)	Thymol		
No.	Solvents	Distilled water	Ethanol solvent	Distilled water	Ethanol solvent	
1.	Alkaloids					
	1. Dragendorff's test	+	+	+	+	
	2. Mayer's test	+	+	+	+	
	3. Hager's test	+	+	+	+	
2.	Carbohydrates					
	1. Fehling's test	+	-	+	-	
	2. Molisch's test	-	+	-	+	
3.	Flavonoids					
	1. Alkaline reagent test	+	+	+	+	
	2. Shinoda's test	+	-	+	+	
4.	Phenol					
	1. FeCl <sub>3</sub> test	+	+	+	+	
	2. Lead acetate test	+	-	+	-	
5.	Glycosides					
	1. Borntrager's test	+	+	+	+	
	2. Keller-Killiani's test	-	+	+	+	
6.	Terpenoids					
	Salkowski's test	+	+	+	+	
7.	Steroids					
	Liebermann Burchard's test	+	+	+	+	
8.	Proteins and Amino acid					
	1. Ninhydrin's test	-	+	-	+	
	2. Biuret's test	+	+	+	+	

The (+) sign signifies the presence of phytochemicals, whereas the (-) sign signifies their absence in the TVLE and thymol.

S. No.	No. of Groups	Treatment Drug	Conc. (mg/kg)	Locomotor activity in 10 min		% Change in
				Before	After	activity
1.	Control-I	Control + Apomorphine	2.5mg/kg	294.5 ± 16.69	281.23 ± 11.43	13.27
2.	Standard-II	Diazepam + Apomorphine	5mg/kg+ 2.5mg/kg	289.56 ± 6.23	145.96 ± 3.25	49.59***
3.	Test Group-III	Aripiprazole+TVLE	1mg/kg+50mg/kg	287.51 ± 9.17	190.12 ± 2.34	37.35*
4.	Test Group-IV	Aripiprazole+ TVLE	1mg/kg +100mg/kg	299.50 ± 10.62	162.60 ± 2.49	45.70**
5.	Test Group-V	Aripiprazole+ Thymol	1mg/kg +5mg/kg	298.44 ± 12.20	133.16 ± 3.19	55.38***

Table 2. The effect of TVLE and thymol in locomotor activity by using an Actophotometer

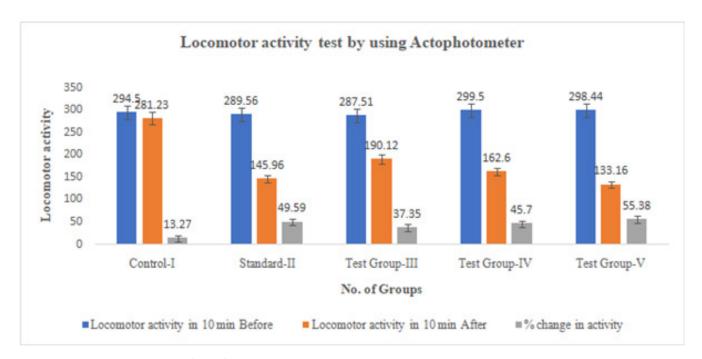


Figure 2. The effect of TVLE and thymol in locomotor activity by using an Actophotometer.

body. In this study, TVLE and thymol enhanced the locomotor activity in the treated mice. TVLE and thymol can be a better profile for a locomotor effect than diazepam because they inhibit locomotor activity less severely.

The effect of TVLE and thymol were compared with that of the control group and the standard group received diazepam (5mg/kg) treated with apomorphine (2.5mg/kg) in mice. All the values were expressed in mean ±SEM of six mice in each group. For a given portion, Significant values were presented at \*p<0.05, \*\*p<0.01 and \*\*\*p<0.001.

The results found that TVLE and thymol showed a significant increase in locomotor activity and % change in locomotive response when compared to the control and the standard groups (Figure 2).

The observed total % change in activity was plotted against the different concentrations of test drugs in each group. Pre-treatment with TVLE and thymol showed significant (\*\*\*p<0.001) inhibition of locomotory effects and gross behavioural changes in this experiment. Additionally, it also decreased the movement in treated mice in chlorpromazine-induced locomotor effect in a significant manner (\*\*p<0.01).

### 4.4 Anti-Schizophrenic Activity

# 4.4.1 Inhibition of Apomorphine-Induced Climbing Time in Mice

Treatment with TVLE and thymol on antipsychotic activity by apomorphine climbing inhibition in mice model causes the dopamine transporters inhibition as per previous reports. The inhibition

of apomorphine at 2.5mg/kg (s.c.) climbing in mice was estimated by the standard drug risperidone at 0.2mg/kg (i.p.). There was a significant (\*\*\*p<0.001) reduction in the apomorphine climbing inhibition in experimental mice. *In vivo* animal screening model of antipsychotic activity, it was estimated that the appropriate concentration of test drug TVLE and thymol at doses of (50, 100 mg/kg, i.p. and 5mg/kg, i.p. respectively) when given with aripiprazole, it is significantly (\*\*p<0.01) decreased the total no. of time spent in apomorphine climbing in mice (Table 3). Animals' behavioural reactions to the dopamine agonist apomorphine were compared to those of the control group Table 3 (Figure 3).

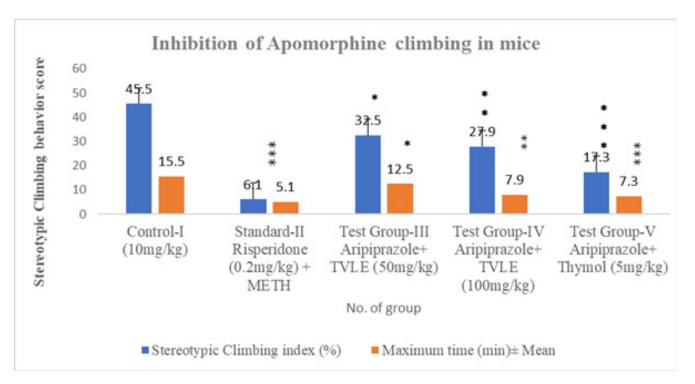
The effect of TVLE and thymol in the climbing test apparatus were compared with that of the standard group that received Risperidone (0.2mg/kg) treated with Apomorphine (2.5mg/kg) in the animal's model. The results were shown as the mean ±SEM of six mice for each group for each value. Non-significant (NS) and significant at value were presented at \*p<0.05, \*\*p<0.01, and \*\*\*p<0.001.

The results were shown as the mean  $\pm$ SEM of six mice for each group for each value. Non-significant (NS) and significant at value were presented at \*p<0.05, \*\*p<0.01, and \*\*\*p<0.001.

The results found that there was a significant interaction between apomorphine-used disorders

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S. No.	No. of Groups	Treatment Drug	Concentration (mg/kg)	Stereotypic Climbing Index (%)	Maximum time (min)± Mean
1.	Control Group-I	Control treated with Apomorphine	2.5mg/kg	45.5 ± 3.7 <sup>NS</sup>	15.5± 0.7 <sup>NS</sup>
2.	Standard Group-II	Risperidone+ METH	0.2mg/kg +5mg/kg	6.1 ± 1.5***	5.1 ± 0.5***
3.	Test Group-III	Aripiprazole+ TVLE	1mg/kg+50mg/kg	32.5 ± 2.8*	12.5 ± 0.8*
4.	Test Group-IV	Aripiprazole+ TVLE	1mg/kg +100mg/kg	27.9 ± 2.1**	7.9 ± 0.1**
5	Test Group-V	Arininrazole± Thymol	1ma/ka ±5ma/ka	173 +1 4***	73+04***

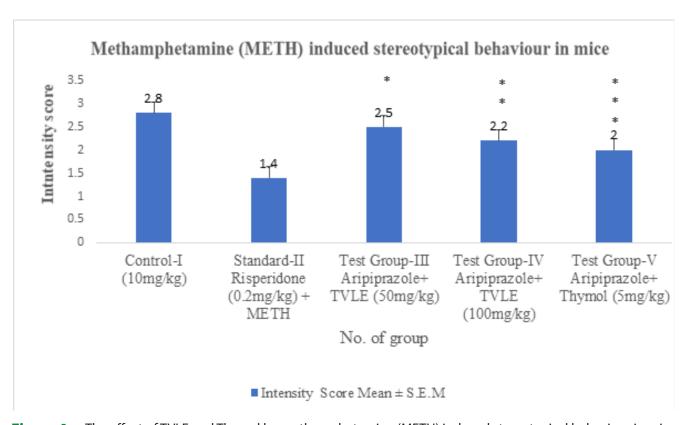
Table 3. The effect of TVLE and thymol by inhibition of Apomorphine climbing mice



**Figure 3.** The effect of TVLE and Thymol by inhibition of Apomorphine climbing in mice.

		, ,		* *
S. No.	No. of Groups	Treatment Drug	Concentration (mg/kg)	Intensity score Mean ± S.E.M
1.	Control Group-I	Control treated with METH	10mg/kg	2.8± 0.13 <sup>NS</sup>
2.	Standard Group-II	Risperidone + METH	0.2mg/kg +10mg/kg	1.4± 0.16***
3.	Test Group-III	Aripiprazole + TVLE	1mg/kg+50mg/kg	2.5± 0.15*
4.	Test Group-IV	Aripiprazole + TVLE	1mg/kg +100mg/kg	2.2± 0.15**
5.	Test Group-V	Aripiprazole + Thymol	1mg/kg +5mg/kg	2.0± 0.00***

Table 4. The effect of TVLE and thymol by methamphetamine (METH) induced stereotypical behaviour in mice



**Figure 4.** The effect of TVLE and Thymol by methamphetamine (METH) induced stereotypical behaviour in mice.

which was standardized by the antipsychotic drug risperidone at a dose of 0.2 mg/kg (i.p.) on the occurrence of antipsychotics activity and observation of the parameters of sniffing, licking repetitive locomotion, twirling, biting, circling, and head-nobbing.

# 4.4.2 Methamphetamine (METH) Induced Stereotype Behaviour in Mice

The effect of TVLE and thymol in different doses when treated with aripiprazole, reduced the stereotypes in treated mice induced by methamphetamine. The standard drug risperidone at 0.2mg/kg i.p. significantly reduced stereotyped behaviour (Table 4). Scoring was

based on the position of the paws at each inspection time to obtain the total score (maximum score of 20). The recorded observations were stereotypes of licking, biting, and other facial abnormal actions that showed involvement of schizophrenia, characterized mainly by distinctive striatal subregions with dopamine neurotransmission Table 4 (Figure 4).

The effect of TVLE and thymol were compared with that of the control group and the standard group received Risperidone (0.2mg/kg) treated with METH (10mg/kg) animals. All the values were expressed in mean ±SEM of six mice in each group. For a given

portion, Non-significant (NS) and significant values are presented at \*p<0.05, \*\*p<0.01 and \*\*\*p<0.001.

Figure 4 shows the effect of TVLE and Thymol by methamphetamine (METH) induced stereotypical behaviour in mice.

The observed total scores were plotted against the different drugs given in each group. Pre-treatment with TVLE and thymol (50, 100 mg/kg, i.p. and 5mg/kg, i.p. respectively) significantly (\*\*\*p<0.001) inhibited the methamphetamine-induced stereotypy behaviour in a dose-dependent manner. Additionally, it also decreased methamphetamine-induced climbing time in a significant (\*\*p<0.01) manner.

Stereotype and climbing time caused by methamphetamine in mice was reversed by the administration of risperidone (0.2mg/kg, i.p.).

The results found a significant interaction between methamphetamine-induced disorders and the standardized antipsychotic drug risperidone on the occurrence of antipsychotic activity and the climbing behaviour in experimental mice.

#### 5. Conclusion

Schizophrenia is a neuropsychiatric condition which is chronic, persistent and significantly showing a serious mental disorder in which reality is seen by sufferers strangely. The phytoconstituents present in TVLE and thymol were terpenoids, phenols and flavonoids which are essential parts having anti-Schizophrenic properties. The present study results indicated the anti-dopaminergic-like effect of *Thymus vulgaris* and its bioactive moiety of thymol in treated mice, suggesting that thymol has antipsychotic-like properties that can be used to treat mental health-related issues.

It was concluded from the present research work that the evaluation of the ethanol extract of *Thymus vulgaris* (leaves) and its bioactive constituent thymol bears significant anti-schizophrenic activity along with essential components required for minimizing schizophrenic symptoms. To effectively use these chemicals in the treatment of diverse forms of mental illnesses, further research will be required for the management of psychotic disorders by describing their target sites and elaborating molecular mechanisms in detail.

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#### 7. References

- Westh H, Zinn SC, Rosdahl VT, Sarisa Study Group. An international multicenter study of antimicrobial consumption and resistance in *Staphylococcus aureus* isolates from 15 hospitals in 14 countries. Microbial drug resistance. 2004; 10(2):169-76. https://doi. org/10.1089/1076629041310019 PMid:15256033
- Cassileth, Barrie R. Complementary therapies: The American experience. Supportive care in cancer. 2000; 8:16-23. https://doi.org/10.1007/s005209900036 PMid:10650892
- 3. Patel, Krishna R, Cherian J, Gohil K, Atkinson D. Schizophrenia: overview and treatment options. Pharmacy and Therapeutics. 2014; 39(9):638.
- Kirkbride, James B, Fearon P, Morgan C, Dazzan P, Morgan K, Tarrant J, Lloyd T, et al. Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study. Archives of general psychiatry. 2006; 63(3):250-8. https://doi.org/10.1001/archpsyc.63.3.250 PMid:16520429
- Picchioni, Marco M, Rijsdijk F, Toulopoulou T, Chaddock C, Cole JH, Ettinger U, Oses A, Metcalfe H, Murray RM, and McGuire P. Familial and environmental influences on brain volumes in twins with schizophrenia. Journal of Psychiatry and Neuroscience. 2017; 42(2):122-30. https://doi.org/10.1503/jpn.140277 PMid:28245176 PMCid: PMC5373701
- Jose, Sonja, Jaykar B. Isolation, Characterization, and phytochemical evaluation of active compound thymol from *Cyclea peltata* (Lam). Nveo-natural volatiles & essential oils journal nveo. 2021:10803-12. https://doi.org/10.9734/ jpri/2021/v33i44A32619
- Hanan OA, Abdel-Rahman RF, Elbaset Mohamed MA, Ahmed-Farid OA, Khattab MS, Abd-Elsalam RM. Thymol ameliorated neurotoxicity and cognitive deterioration in a thioacetamide-induced hepatic encephalopathy rat model; involvement of the BDNF/CREB signalling pathway. Food and Function. 2022; 13(11):6180-94. https:// doi.org/10.1039/D1FO04292K PMid:35583008
- Amzad MH, AL-Raqmi AS, Al-Mijizy ZH, Mohammed Weli
  A, Al-Riyami Q. Study of total phenol, flavonoids contents
  and phytochemical screening of various leaves crude
  extracts of locally grown *Thymus vulgaris*. Asian Pacific

- journal of tropical biomedicine. 2013; 2(9):705-10. https://doi.org/10.1016/S2221-1691(13)60142-2PMid:23998010
- Shaban, Nema S, Tohamy MA, El-Banna HA, Abeer MR, El-Gendy AA, Asmaa O. Phytochemical and pharmacological studies of ethanolic extract of *Thymus vulgaris*. World Journal of Pharmacy and Pharmaceutical Sciences. 2015; 4(10):1988-2001.
- 10. Asha D, Mathew L. Chemical profiling of *Thymus vulgaris* L. using HPTLC. Journal of Pharmacognosy and Phytochemistry. 2017; 6(4):1017-23.
- Carolina C, Moreno-Arribas MV, Pedro J. Martín-Álvarez, Bills G, Vicente FM, Basilio A, López Rivas C, Requena T, Rodríguez JM, Begoña Bartolomé. Antimicrobial activity of phenolic acids against commensal, probiotic and pathogenic bacteria. Research in microbiology. 2010; 161(5):372-82.https://doi.org/10.1016/j.resmic.2010.04.006 PMid:20451604
- 12. Semma HS, Halail AT, M. Hamed FM, Hassan BA. Maceration techniques extraction of *Thymus vulgaris* and Laurel (*Laurus nobilis*) leaves with antibacterial study. Plant Archives. 2019; 19(2):4041-4.