# **Original paper**

# **Antinociceptive Effect of Peppermint in Mice**

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# Abstract

**B** ackground: Menthol the primary component of the essential oil of peppermint is thought to be responsible for most of its properties. It is thought to provide a local anesthetic action and be of use in musculoskeletal pain, but with no experimental evidence for analgesic activity with respect to the leaves of this plant.

**Methods:** Forty Swiss mice of either sex (weighing 20-25grams) was used in this study, divided into five groups each with eight animals. Group 1: receiving distilled water. Groups 2, 3&4: pre-treated with aqueous extract of peppermint in doses 50, 75 and 100 mg/kg, orally Respectively, and Group 5: pre-treated with standard drug (Ibuprofen 100 mg/kg), orally. The analgesic activity was determined by radiant heat Tail-flick method in mice and converted (using special equation) to maximum possible effect. The results are reported as mean  $\pm$  S.E.M and analyzed with ANOVA followed by Dunetts multiple comparison test. The results were significant at p<0.05.

**Results:** The Maximal Possible Effect (%MPE) was significant when peppermint was used in a dose of 100mg/kg, and not significant when was used in doses of 50mg/kg &75mg/kg as compared to % MPE of Ibuprofen.

**Conclusion:** Peppermint has analgesic effect when given orally as aqueous extract of dried leaves in a dose of 100mg/kg in mice.

Keywords: Peppermint, analgesic activity, aqueous extract, & maximum possible effect.

# Introduction

commonly Mentha piperita called Peppermint is thought to be a natural hybrid between spearmint (Mentha *spicata*) and water mint (*Mentha aquatica*) <sup>(1)</sup>, Peppermint oil is used to relieve menstrual cramps & used externally for neuralgia, myalgia, headaches. & migraines <sup>(2)</sup>.

Menthol is the primary component of the essential oil of peppermint. It occurs naturally as a colorless crystal or powder <sup>(3)</sup>. Menthol is mostly responsible for the spasmolytic nature of peppermint. It stimulates bile flow, reduces the tone in the esophageal sphincter, facilitates belching, and has antibacterial properties <sup>(4)</sup>. It is used as a local anesthetic agent in cold and cough preparations and in liniments for insect bites, eczema, poison

ivy, hemorrhoids, toothaches, and musculoskeletal pain. It is used as an antitussive in chest rubs or inhaled as a steam vapor <sup>(5)</sup>. Its use dates back to 1890, when it was developed as a topical rub to treat whooping cough. It is thought to provide a local anesthetic action on the lungs and throat, suppressing the cough reflex <sup>(6)</sup>.

There is no experimental evidence for analgesic activity with respect to the leaves of this plant <sup>(7)</sup>. Hence, in the present study, an attempt was made to investigate the analgesic effects of the aqueous extract of dried leaves of *Mentha piperita* in experimental animals.

# Materials & Methods

Animals: The study was performed using 40 Swiss mice of either eight weighing 20-

25g. They were kept at room temperature allowing food and water *ad libitum* and were exposed to normal day and night light cycles. The experimental animals were divided randomly into five groups with 8 animals in each group (n=8).

Group 1 (D.W.) receiving distilled water. Groups 2, 3&4 (pre-treated with aqueous extract of peppermint in doses 50, 75 and 100 mg/kg, orally, respectively). Group 5 (Ibuprofen) pre-treated with standard drug Ibuprofen 100 mg/kg, orally.

**Preparation of the aqueous extract:** *Mentha piperita* leaves were obtained from local market; after approval by taxonomist, Aqueous extraction was performed by adding 200 ml of boiling water to 200 mg of *Mentha piperita* dried leaves then ; wait for the solution to become cold; the extract filtered and leaved for evaporation until 100 ml to obtain a concentration of 200mg/100ml.

**Dose calculations:** Three doses of the *Mentha piperita* aqueous extract were used in this study, 50mg/kg, 75mg/kg and 100mg/kg which were calculated according to mice body weight to be equivalent to corresponding volume of aqueous extract of stock solution 2mg/ml.

Tail flick test: Tail flick method: The analgesic activity was determined by radiant heat Tail-flick method in mice<sup>(8)</sup>. Ibuprofen (100 mg/kg orally) was used as standard drug. Tail-flick latency was assessed by the analgesiometer (Inco, India). The strength of the current passing through the naked nichrome wire was kept constant at 5A. The distance between heat source and the tail was 1.5 cm and the application site of the heat on the tail was within 2 cm, measured from the root of the tail. Cut-off reaction time was 10s to avoid any tissue injury during the process. Tail-flick latency was measured after 1h of the administration of the drug/extract. Tail flick latencies were converted to maximum possible effect (MPE), according to the following formula:

MPE (%) =  $100 \times$  (post-extract latency - pre-extract latency) / (cut-off time - pre-extract latency).

#### Statistical analysis

The results are reported as mean  $\pm$  S.E.M and analyzed with ANOVA followed by Dunetts multiple comparison test. p<0.05 are considered significant.

# Results

The analgesic effect of the aqueous extract of peppermint is shown in Table 1 & figure 1. The extract at dose of 50mg/kg showed 14.38% of Maximal Possible Effect (%MPE) after 3 hours of oral intake, and showed 31.74% of Maximal Possible Effect (%MPE) after 3 hours of oral intake of 75mg/kg. Whereas the extract at the dose of 100 mg/kg orally showed 39.59% of Maximal Possible Effect (%MPE) which was comparable to standard drug, ibuprofen which showed 43.63% of Maximal Possible Effect at dose of 100 mg/kg, orally.(p<0.05).

# Discussion

Antinociceptive effect of orally administered aqueous extract of dried leaves of peppermint was demonstrated in this study by Tail flick test. The peppermint aqueous extract was given orally in three doses (50, 75 & 100 mg/kg) as shown in table 1& figure 1, and compared to a well known analgesic drug (Ibuprofen). The peppermint is well known to be effective at a dose of 75mg/kg <sup>(11&12)</sup>. So, in this study a dose below (50mg/kg) and a dose above (100 mg/kg) the effective dose were taken to elicit the most suitable doses needed to produce the analgesic effect. In the table 1, we can see that the Maximal Possible Effect of peppermint at dose of 50 mg/kg was not significant at 1, 2 & 3 hours after oral intake of the herb. Where as, at a dose of 75 mg/kg, the Maximal Possible Effect was significant after 2 & 3 hours of the oral intake but not in the fist hour. This can be explained by the fact that peppermint is well known to be effective at a dose of 75mg/kg, but its effect needs more time to be shown <sup>(13-15)</sup>. Finally, at a dose of 100mg/kg, peppermint can produce Maximal Possible Effect similar to that produced by a well known analgesic drug (Ibuprofen), as the results were significant at 1,2 &3 hours after oral intake of the aqueous extract. The fact that peppermint can act as an analgesic remedy when used in high dose can be supported by several studies which referred to this ability of that herb <sup>(14-16)</sup>.

However, further work for the isolation of active constituents and elucidating the exact mechanism underlying the observed pharmacological effects is recommended.

### Conclusion

*Mentha piperita* has analgesic activity when its aqueous extract of dried leaves is given orally to mice in a dose of 100mg/kg.

Groups		% Maximum Possible Effect		
	Dose (mg/kg)	1hr	2hr	3hr
Group 1 (D.W.)	0.0	0.00	0.00	0.00
Group 2 (Peppermint)	50	8.19±0.42	12.22±0.22	14.38±0.54
Group 3 (Peppermint)	75	13.49±0.26	22.19±0.47*	31.74±0.15*
Group 4 (Peppermint)	100	19.99±0.29*	34.19±0.39*	39.59±0.28*
Group 5 (Ibuprofen)	100	20.05±0.21*	37.39±0.69*	43.63±0.47*

Table 1. Analgesic activity of peppermint on tail-flick assay of mice

Values are Mean ±SEM (n=8); one way ANOVA.

\*p<0.05 compared to control.



**Fig. 1.** Percentage of Maximum Possible Effect of different doses of peppermint compared to D.W. & Ibuprofen at 1, 2 & 3 hours after oral intake.

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