Original paper

Antinociceptive Effect of Peppermint in Mice

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Background: Menthol, which is primary component of the essential oil of peppermint, is thought to be accountable for most of peppermint properties. It is also thought to have an anesthetic action locally and be of use in musculoskeletal pain, but with no experimental evidence for analgesic activity regarding its leaves.
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 orally with aqueous extract of peppermint in doses 50, 75 and 100 mg/kg, respectively. Group 5: pre-treated with standard Ibuprofen drug 100 mg/kg, orally. The analgesic activity was determined using radiant heat Tail-flick method in mice and converted (using special equation) to maximum possible effect. The results are reported as mean ± 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: Aqueous extract of dried leaves of Peppermint has analgesic effect when given orally in a dose of 100mg/kg in mice.
Keywords: Peppermint, analgesic activity, aqueous extract, & maximum possible effect

Introduction

Mentha piperita commonly called Peppermint is believed to be a natural hybrid of spearmint *(Mentha spicata)* and water mint *(Mentha aquatic)*. [1] Peppermint oil is used to relieve menstrual cramps & used externally for neuralgia, myalgia, headaches, & migraines [2].
Menthol considers as a primary component of the essential oil of peppermint that occurs naturally as a colorless crystal or powder [3].The spasmolytic nature of peppermint is mostly attributed to Menthol .The stimulates bile flow of Menthol can reduce the tone in the esophageal sphincter, facilitates belching, and has antibacterial Properties [4]. It has been used as a local anesthetic agent in cold and cough preparations. It has been also utilized in liniments for insect bites, eczema, poison ivy, hemorrhoids, toothaches, and musculoskeletal pain. Moreover, it has been used as an antitussive in chest rubs or inhaled as a steam vapor [5]. In 1890, Menthol was first used as a topical rub to treat whooping cough, where it is believed to act as a local anesthetic agent on the lungs and throat, suppressing cough reflex [6].

There is no experimental evidence for analgesic activity of the leaves of this plant [7]. Hence, in this 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*

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libitum with exposure to normal day and night light cycles. These experimental animals were randomly divided into five groups of 8 animals in each group (n=8).
Group 1 (D.W.) receiving distilled water. Groups 2, 3&4 were pre-treated orally with aqueous extract of peppermint in doses 50, 75 and 100 mg/kg, respectively. Group 5 (Ibuprofen) was pre-treated orally with standard Ibuprofen 100 mg/kg drug.

Preparation of the aqueous extract:

Mentha piperita leaves were obtained from local market; after approval by taxonomist, Aqueous extraction was achieved by adding 200 ml of boiling water to 200 mg of *Mentha piperita* dried leaves. This was allowed 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 [8]. 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 heat source was1.5 cm away from the tail and the application site of the heat on the tail was within 2 cm, which measured from the root of the tail. In order to avoid any tissue injury during the process, the Cut-off reaction time was 10s. Tail-flick latency was determined after 1h of the administration of the drug/extract, then converted to maximum possible effect (MPE), using the following formula:

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

Statistical analysis

Results are reported as mean ± S.E.M and analyzed with ANOVA. This was compared using 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. Where as the extract at the dose of 100 mg/kg orally showed 39.59% of Maximal Possible Effect (%MPE). This result was comparable to standard drug, ibuprofen that 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 [11&12]. So, in this study a dose below (50mg/kg) and a dose above (100mg/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 75mg/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 [13-15]. 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 [14-16].

However, further studies are needed to investigate the possibilities of isolating the active constituents and elucidating the exact mechanism underlying the observed pharmacological effects.

Conclusion

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

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

Groups	Dose (mg/kg)	% Maximum Possible Effect		
		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*

Values are Mean ±SEM (n=8); one way ANOVA.
*p<0.05 compared to control.

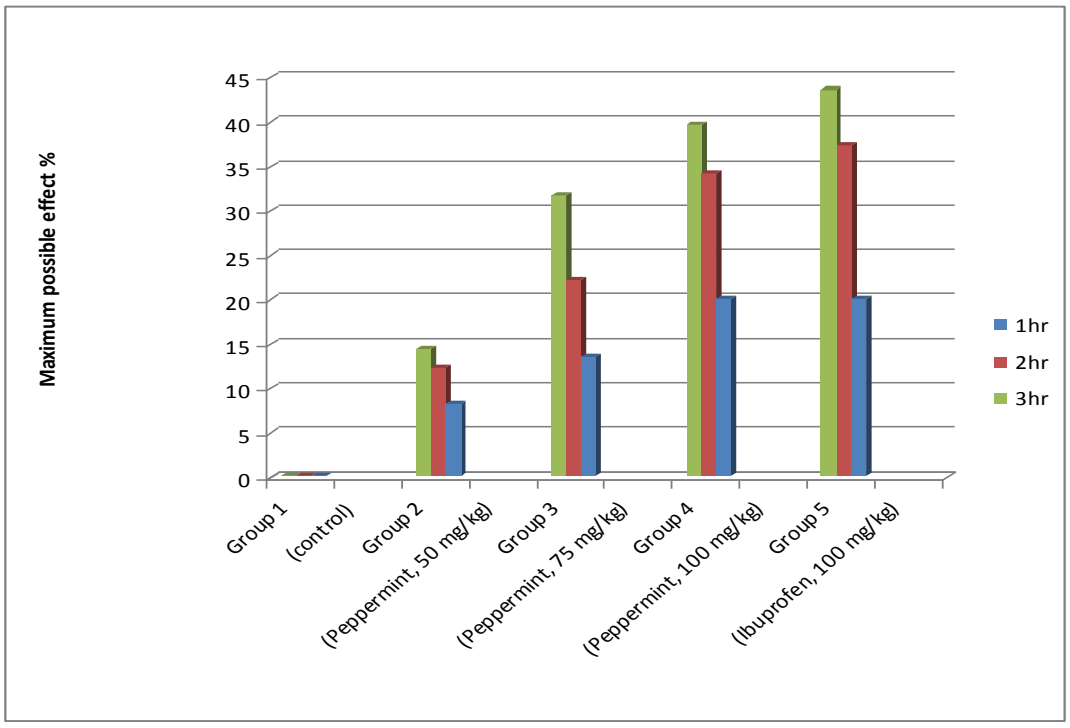

Figure 1. Percentage of Maximum Possible Effect of different doses of peppermint compared to D.W. &Ibuprofen at 1, 2 &3 hours after oral intake.

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