

# Homoeopathic pathogenetic trial of *Mentha piperita* L.: A multi-centric, double-blind, randomised and placebo-controlled trial

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## Abstract

**Introduction:** *Mentha piperita* L, a lesser-known and partly proved drug in homoeopathy, is used extensively as a herbal medicine. **Objective:** The objective of this study is to elicit the pathogenetic response of *Mentha piperita* in comparison to placebo. **Materials and Methods:** A multi-centre, double-blind, placebo-controlled and randomised clinical trial was carried out at three centres with 46 relatively healthy provers. After randomisation, 32 provers were given verum in 6C, 12C, 30C and 200C potencies and in the placebo group, 14 provers were administered identical, un-medicated globules. All the changes were recorded by the provers and elaborated by proving masters. The data were finally processed at proving-cum-data processing cell. **Results:** Out of the 32 provers of the Verum group, 22 reported 61 symptoms, whereas 24 symptoms were reported by seven provers in the placebo group. The majority of the symptoms were produced in the sphere of the locomotor system, followed by the gastro-intestinal system beside other systems. Altogether, ten new Grade I symptoms were identified, while 11 symptoms were similar to those found in the previous literature. **Conclusion:** *Mentha piperita* revealed a significant pathogenetic response in this trial which verifies its previously observed symptoms. Among the newly developed symptoms, two symptoms showed opposite character when compared to the previous literature. Also, statistically significant difference was found in differential eosinophil count in the verum group pre-post intervention. These are the findings that need to be clinically verified to enhance the scope of their clinical use.

**Keywords:** Clinical trial, Mentha, Pathogenetic trial, Peppermint, Proving

## INTRODUCTION

Proving of drugs on healthy humans is a unique process in homoeopathy,<sup>[1]</sup> also known as homoeopathic pathogenetic trial.<sup>[2]</sup> Drug proving research is a flagship program of the Central Council for Research in Homoeopathy (CCRH), the objective of this research is to introduce new drugs of indigenous systems into homoeopathy and to re-prove existing partially proved drugs.<sup>[3,4]</sup> A thoroughly designed drug proving protocol would ensure that the investigational substance is proved sufficiently to evolve the pathogenesis which can later be verified clinically and simultaneously maintaining the quality and minimising the bias in the study.<sup>[5]</sup> *Mentha piperita* L. is a lesser-known drug in homoeopathy and is well known as herbal medicine. Therefore, *Mentha piperita* was included in the program to ascertain its prescribing indications.

*Mentha piperita* L. belongs to the family Lamiaceae with synonyms *Mentha hircine* Hull and *Mentha officinalis* Hull. It is commonly known as peppermint in English, Menthe poivree in French and Pfefferminze in German. In Indian languages Hindi, Bengali, Gujarati, Punjabi, Urdu, Marathi, Tamil and Telugu it is known as Pudina, in Kashmiri and Malayalam, it is known as *Pudyanu* and *Puthina*, respectively. *Mentha piperita* L. is commonly found in India, Europe, Africa, North America and Japan.<sup>[6,7]</sup>

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## Botanical description

*Mentha piperita* L. is a rhizomatous erect perennial herb of 30–90 cm height. The young stem is hairy, green and quadrangular whereas it turns into smooth, rounded and dark purple in colour at maturity. Leaves are light green or purple-brown in colour, opposite, decussate, 4–9 × 2.5 cm, nearly glabrous, shortly petiolate; ovate-oblong to oblong-lanceolate, margins serrate, apex acute, base rounded or narrow, dark green and smooth above, paler below, with numerous glands sparingly pubescent on vein region. The inflorescence is verticillaster where flowers are arranged in thick terminal spicoid racemes. The calyx is tubular-campanulate, green to dark purple, pubescent and glandular; corolla tubular-campanulate, purple and irregular in shape. The stamens are short, four in number and equal in size; the ovary has a projecting style forming gynobasic style and have bifid stigma. The fruits are very small nut-lets up to 0.5 mm in diameter ellipsoidal in shape and blackish-brown in colour.<sup>[6,8]</sup>

## Homoeopathic preparation

Homoeopathic drug, *Mentha piperita* is prepared from the whole plant, excluding the root part. Initially, it is chopped and pounded to a pulp and weighed. Then, two parts by weight of alcohol are taken, the pulp is mixed thoroughly with one-sixth part of it and the rest of the alcohol is added. Then the whole mixture is stirred well and poured into a well-stoppered bottle. It is then allowed to stand 8 days in a dark and cool place. The tincture is then separated by decanting, straining and filtering. The drug power is 1/6. Dilutions are prepared as directed under Class III of pharmacopoeia.<sup>[9]</sup>

## Medicinal values

The herbal preparation of *Mentha piperita* is used in cosmeceutical, personal hygiene products, food and pharmaceutical products for both its flavouring and fragrance properties. It is also used in aromatherapy, mouthwashes, bath preparations, toothpastes and topical preparations. Topical preparations of *Mentha piperita* oil have been used to calm pruritus and relieve irritation and inflammation.<sup>[10]</sup> *Mentha piperita* extract, oil and leaves are used in many cosmetic formulations and found to be very safe.<sup>[11]</sup>

*Mentha piperita* is commonly used in the treatment of abdominal pain, nausea, irritable bowel syndrome and symptomatic relief of cough and cold in children. Peppermint oil vapour was historically used as an inhalant for relieving respiratory congestion. Peppermint oil-infused tea is used to treat cough, bronchitis and inflammation of the oral mucosa and throat. It has been traditionally used for several digestive complaints like indigestion, colic of infants, flatulence, diarrhoea, nausea and vomiting, anorexia and morning sickness.<sup>[12]</sup>

## Homoeopathy uses

The initial proving of *Mentha piperita* was conducted by Dr. Demeures of France, who took a single drop of the tincture and the effects of which lasted into the 3<sup>rd</sup> month.<sup>[13,14]</sup> Marked action of this drug was found on respiratory organs and skin, it

stimulates the cold-perceiving nerves, so just after taking it, a current of air at ordinary temperature may seem cold, as mentioned in *Materia Medica*.<sup>[15]</sup> It is remarkably helpful in dry cough caused by irritation of the respiratory passage or by the air going into the larynx during an effort to talk and hence it is very similar to *Rumex crispus* to its action. The voice is husky, throat feels dry and sore, as if pins were laid crosswise in it. The trachea is painful to touch.<sup>[16]</sup> According to Richard Hughes *Mentha piperita* is very useful in dry coughs, like *Arnica* in injuries and *Aconite* in inflammatory complaints. He wrote that a single dose comprising of one globule of the 30<sup>th</sup> potency was always sufficient whenever there was dry cough even of long duration. *Mentha piperita* seems an analogue of *R. crispus* in its relation to cough.<sup>[17]</sup>

This study aimed to elicit the pathogenetic effects of the drug *Mentha piperita* in different homoeopathic potencies on apparently healthy human beings.

## MATERIALS AND METHODS

### Study design

This is a multi-centre, prospective, parallel-arm, randomised, placebo-controlled and double-blind study where allocation of verum:placebo is 70:30.

### Study setting

The study was conducted at three peripheral centres of the Council, namely: Homoeopathic Drug Research Institute (HDRI), Lucknow (Uttar Pradesh); Drug Proving Unit (DPU), Bhubaneswar (Odisha) and Regional Research Institute for Homoeopathy (RRIH) and Gudivada (Andhra Pradesh).

### Proving period

The proving period was approximately 1 year, from April 2015 to March 2016 in all the centres.

### Sample size

As per the drug proving protocol,<sup>[5]</sup> there should be a minimum of 30 provers in and at least 15 provers at one centre, of which 30% should be in the control group.

### Subjects

A total of 56 volunteers were screened and 46 were enrolled: 15 volunteers each were recruited from HDRI, Lucknow and RRIH, Gudivada and 16 volunteers from DPU, Bhubaneswar. Most of the enrolments were from the students of homoeopathic medical colleges.

### Inclusion and exclusion criteria

Individuals of more than 18 years of age of either sex, found suitable in pre-trial medical examination (PME) and certified as apparently healthy by consultants from the conventional system of medicine, intelligent enough to carefully record the facts and have not taken any homoeopathic medicine in the past one month were included in the study.

The volunteers, who were suffering from any acute or chronic disease, anxiety or hysteria, colour blindness, having any addictions, undergoing any medical treatment, undergone

any surgery in the past 2 months, women during pregnancy, puerperium or lactation and volunteers who have participated in another clinical or proving trial during the past 6 months were excluded from the study.

### Screening and enrolment

Initially, a basic screening was carried out for all the volunteers. The baseline characteristics of each volunteer were enquired in detail, they were also examined thoroughly in respect to every system and detailed laboratory investigations were carried out and noted in specified PME proforma. This was done at each of the centres by the Proving Master/Site Investigator and the Consultants from the conventional system of medicine to ensure the health status of the volunteers after obtaining written informed consent from them. After screening, total of 46 volunteers were enrolled for this study. Enrolment was followed by randomisation.

### Randomisation

Randomisation was done online using randomizer.org at the nodal centre for drug proving in the headquarter level and provers were categorised into two groups, that is, Verum ( $n = 32$ ) and Placebo ( $n = 14$ ) in the allocation ratio of 2:1. Simple randomisation method was used to randomise.

### Blinding and coding

The study, being a double-blind study, the blinding was done at the headquarter level, the study medication is given in coded form as per the randomisation chart. The coded drugs were sent to the study sites, the site investigators and the participants at the study site were kept blind about the nature of the drug substance and the allocation of participants in the verum and placebo groups. The nature of the proving substance was only known to the PI and the Co-I, but the site investigators and the participants were blind to the nature of the Investigational Proving Substance (IPS). The coded study medication was labelled with the Unique Identity Code for the provers and provided to the Site investigator.

### Proving procedure and data recording

All 46 provers were subjected to five phases of proving at each of the centres. In each phase, 12 doses of the coded drug or placebo as per randomisation chart were administered, divided into 4 doses/day for 3 days (if no symptom/sign arises) and provers were asked to stop taking further doses as soon as any symptom or sign appears. Each dose is comprised of four globules of size 30.

All the provers were administered placebo in Phase I for intra-prover response (the response of individual prover to placebo and medicine). In Phases II, III, IV and Phase V, the Verum group received the coded drug in 6C, 12C, 30C and 200C potencies, respectively, whereas the placebo group received optically identical placebo, which was also identical in taste and smell.

The provers enrolled in the study were supervised by a proving master at each study centre. The provers were asked

to note down the details of their feelings/changes in mental and/or physical level daily, after taking the doses of the coded drug and in the subsequent was out period of 30 days in the 'Prover's Day Book Proforma.' If sign(s)/symptoms(s) appeared, the sequence of the appearance of new sign(s) and/or symptoms(s) along with the date, time of onset and duration for which they persisted were noted. The entries made by the provers were completed with respect to their location(s), sensation(s), modalities and concomitants. The extension of symptoms, causation, clinical and pathological findings (if any) was written in the 'Symptom Elaboration Pro forma' by the Proving Master/Site investigator. In case of any distressing symptom or any illness occurring during trial and treatment taken (if any) is also noted in the same pro forma. But as this is considered as an adverse event, a separate form for reporting the adverse event is filled and reported as per the protocol.

If no sign(s)/symptoms(s) appeared after taking all the 12 doses of the coded drug, the provers mentioned as such in the pro forma and observed a 30 days washout period, before starting the intake of the next potency of the drug.

After completion of the trial with all potencies, the provers underwent post-trial or terminal medical examination (TME) in the same manner as done during PME. The compilation of data recorded in the 'Prover's Day Book pro forma,' 'Symptoms Elaboration Pro forma,' 'Investigation Reports – Pre and Post trial' and 'Adverse event reports,' if any was done by the drug proving-cum-data processing cell.

### Intervention

#### Verum group

*Mentha piperita* in 100 ml sealed bottles of 6C, 12C, 30C and 200C potencies were procured from a GMP-certified Homoeopathic drug manufacturer in India. Globules of size 30 were medicated with these attenuations at proving-cum-data processing cell at the Nodal Office of Drug Proving Research Programme of the Council.

#### Placebo group

An optically identical placebo was prepared with un-medicated globules (size 30) moistened with un-succussed dispensing alcohol.

### Pathogenetic symptoms

Pathogenetic symptom can be defined as any change in a normal objective and/or subjective state of mind or body as experienced by the prover, or as observed by the proving investigator and/or others occurring during the proving period, which are possibly related to the IPS.

The sign(s) and/or symptoms(s) produced in provers of Verum (drug) or Placebo (control) group were noted down for each stage with the number of doses, after which each of the sign(s) or symptom(s) appeared and the duration for which they continued. The sign(s) and/or symptom(s) generated by the Verum group and Placebo group were separated. The

sign(s) and/or symptoms(s) which were produced by provers in the Verum as well as Placebo group in Phase I were not considered as pathogenetic symptoms. These symptoms were used for intra-prover and inter-prover assessment to derive the Pathogenetic effect of the drug substance.

### Management of severe symptoms (adverse events)

For identification of adverse events and their management, the Homeopathic Pharmacopeia Convention of the United States guidelines<sup>[18]</sup> were adopted.

### Unblinding and data analysis

Un-blinding or breaking of the randomisation codes was done at the Nodal office after the study was completed at all the study sites. The reporting adheres to the consolidated standards of reporting trials (CONSORT)<sup>[19]</sup> and Reporting data on homeopathic treatments (RedHot): A supplement to CONSORT.<sup>[20]</sup> The data of pathogenetic symptoms and the changes in the laboratory investigations were compiled. The qualitative and quantitative analyses were done for the symptoms generated during the trial. The variables pertaining to the demographic data and laboratory investigations were analysed using independent *t*-test with Statistical Package for the Social Sciences version 20 for Windows (IBM).

### Ethics and consent

The Institutional Ethics Committee of CCRH approved the study protocol and the drug for conducting the trial. Written informed consent was obtained from all the volunteers prior to enrolment in the study. The trial was conducted in accordance with International Conference on Harmonisation Guidelines for Good Clinical Practice, Helsinki Declaration.

### CTRI registration

CTRI/2018/11/016424.

## RESULTS

A total of 56 volunteers were screened and 46 volunteers (24 males and 22 females) were enrolled as provers from three centres. Of these 32 were on verum and 14 were in the placebo group [Figure 1]. The average age of the verum group was  $23.7 \pm 4.69$  years and that of the placebo group was  $26.07 \pm 7.10$  years. The baseline information in both the groups was comparable ( $P \geq 0.05$ ) and well-matched as shown in Table 1.

All the 46 provers participated till the end of the research trial and there were no dropouts. The data analysis was done regarding pathogenetic effects, changes in objective signs and investigational values, such as systolic blood pressure and diastolic blood pressure, haemoglobin percentage (Hb%), differential count of neutrophil (N), eosinophil (E), lymphocyte (L), total white blood cell count, total red blood cell (TRBC) count and serum cholesterol and urea. Urine analysis, Chest X-ray and USG findings noted at the beginning and end of the trial were also compared.

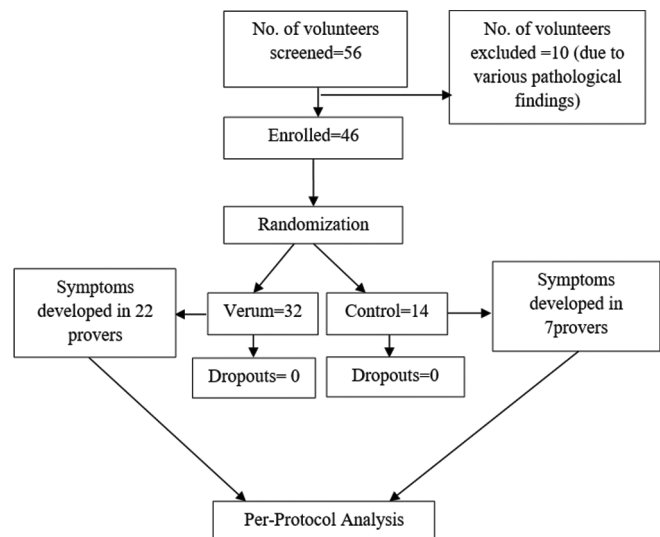


Figure 1: Flowchart of study participation

Table 1: Baseline information

Variable	Verum (n=32) Mean ± SD	Placebo (n=14) Mean ± SD	P-value
Age (years)	23.7±4.69	26.07±7.10	0.1997
Male provers	16	8	
Female provers	16	6	
BMI (kg/m <sup>2</sup> )	22.45±3.85	22.32±4.02	0.9176
SBP (mm Hg)	118.438±6.618	120.500±6.711	0.3382
DBP (mm Hg)	76.938±4.534	77.857±4.258	0.5230
TRBC (cells/cumm)	4.205±0.456	4.539±0.426	0.0245
Hb% (g/dL)	12.359±1.404	13.100±1.443	0.1095
TWBC (cells/cumm)	7589.063±1256.963	7578.571±1143.664	0.1095
DC.N (cells/cumm)	58.031±9.885	56.429±10.493	0.6219
DC.E (cells/cumm)	5.250±2.095	4.286±1.684	0.1363
DC.L (cells/cumm)	35.781±8.746	38.286±11.125	0.4155
ESR (mm/hr)	11.467±5.444	13.286±6.673	0.3359
RBS (mg/dl)	79.919±11.442	79.452±6.966	0.8884
T. Cholesterol (mg/dl)	167.032±27.967	179.500±25.829	0.1619
Urea (mg/dl)	21.250±5.314	22.022±5.938	0.6638

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TRBC: Total red blood cells, DC.N: Differential count neutrophils, DC.E: Differential count eosinophils, DC.L: Differential count lymphocytes, ESR: Erythrocyte sedimentation rate, T. Cholesterol: Total cholesterol, TWBC: Total white blood cell count

### Pathogenetic effects

#### Quantitative analysis

During the trial, in the verum group, 22 out of 32 provers reported 61 symptoms. In the placebo group, seven out of 14 provers reported 24 symptoms.

The overall incidence of pathogenetic effects in this trial (% of provers) was calculated by dividing the number of volunteers

who had at least one reported pathogenetic effect by the total number of volunteers who took the IPS.<sup>[21]</sup> The incidence of pathogenetic effects in this trial was 68.75%.

$$\frac{\text{Number of provers who had at least one reported pathogenetic effect}}{\text{Total number of provers who took the drug}} = \frac{22}{32} \times 100 = 68.75\%$$

The incidence of pathogenetic effects per prover is defined as the total number of findings observed in the trial divided by the total number of provers that produced the symptoms.<sup>[21]</sup> In this trial 61 symptoms were produced by 22 provers. Hence, the incidence of pathogenetic effects per prover in this trial is 2.77.

In this study, *Mentha piperita* produced symptoms in all the administered potencies i.e., 6C, 12C, 30C and 200C. The number of symptoms produced was 17 in 6C potency, 18 in 12C potency and 13 each in 30C and 200C potency.

Out of the 61 symptoms developed in this trial, 18 symptoms were produced by male provers and 43 by female provers.

### Qualitative analysis

The pathogenetic symptoms of *Mentha piperita* developed in this trial were derived after an inter-prover comparison of the symptoms developed in the Placebo group and those produced with different potencies of the Verum group [Table 2].

### Sphere of action

The majority of the symptoms were produced in the locomotor system, followed by the gastro-intestinal system, but the drug also showed action in the sphere of mind, head, eye, ear, respiratory system, urinary system, male and female reproductive systems, sleep and skin.

There were eight symptoms pertaining to the sphere of the head, which developed with all potencies, predominantly by 6C and 12C potencies, in 7 provers.

There were three symptoms of eye produced by 3 provers in 6C and 30C potencies.

Similarly, six symptoms related to the respiratory system were generated in 5 provers, largely with 30C and 200C.

Ten symptoms developed in 6 provers that pertained to the sphere of the gastrointestinal system, with all potencies.

In the locomotor system, fifteen symptoms were produced by 8 provers, with all potencies, but mostly with 12C potency. Pain in extremities, especially 'right sided,' has been produced in 4 provers at two different centres.

In skin, 10 symptoms were produced by 5 provers, with all potencies.

The symptom of sleepiness was produced in four provers of the same centre and one prover has produced this symptom in all four potencies.

The rest of the symptoms were produced in separate individual provers.

### Grading of the symptoms

#### Grade I symptoms

Grade I symptoms are those that appear in more than 2 provers, at two different study sites (Symptom in 1 or more prover at one site and similar symptom in 1 or more provers at the second site, i.e., if two provers separated by distance and, without any mode of contact or communication with each other, give the same symptom) or the peculiar, rare, queer, strange, characteristic symptoms or the symptoms reappearing from prior provings.

'Throbbing pain in forehead' was noticed in 3 provers at three different centres and pain in right frontal region was experienced by 2 provers with 12C potency at different centres.

'Itching in eye' was experienced by 2 provers at the same centre with different potencies. 'Amelioration from the cold application' was also found in eye complaint of 2 provers.

'Obstruction of nose' was found in 3 provers in 2 potencies and it was 'associated with dyspnoea' in 2 of them with 30C potency and both experienced 'amelioration from washing with cold water.'

'Constipation' was noted in two provers at two different centres.

'Cutting pain in lower abdomen' was reported by 2 provers of different centres and cutting pain in left lower abdomen was also reported by one of these provers after a gap of several days and it was associated with leucorrhoea.

One prover developed small red eruptions with itching, aggravated by warmth and in the evening and ameliorated by scratching and cold application, twice over a gap of 3 days, with 6C potency.

Sleepiness was experienced by 6 provers at a single site and one prover developed sleepiness with all four potencies but not with placebo. Sleeplessness/reduced sleep was noticed in 12C potency in one prover of the same centre. Skin symptoms were observed in two provers of two centres after 12C potency.

Aggravation in morning was seen in seven provers as a modality with various symptoms.

Similarly, for seven symptoms related to pain in different parts of the body, the modality amelioration by pressure was noted in 4 provers of two different centres.

The general symptoms like thirst and appetite have shown polarity.

Thus, the following may be considered Grade I pathogenetic symptoms of this drug:

1. Throbbing pain in the forehead (right frontal region)
2. Nasal obstruction with dyspnoea, amelioration by washing with cold water

3. Itching in eyes, amelioration and cold application
4. Constipation
5. Cutting pain in the lower abdomen
6. Small red eruptions with itching, aggravated by warmth, evening and ameliorated by scratching, cold application
7. Sleepiness/Drowsiness (polarity – Sleeplessness/Reduced sleep)
8. General physical symptoms: Appetite reduced, Thirstlessness associated with headache and upper respiratory tract infections; thirst increased in general and during fever
9. General modalities: Aggravation in morning and Amelioration by cold application, pressure
10. Side affinity: Right-sided complaints are more than left side

### Grade II symptoms

Grade II symptoms are all pathogenetic symptoms other than those in Grade I symptoms mentioned above.

Pathogenetic symptoms reflected in Table 2 which developed in a single prover and having no marked characteristics or modalities are considered under this category.

Other findings are as follows:

- Symptoms related to ear, maxilla, aphthae, rectum, male genitalia and back developed in verum group alone
- Symptoms related to pain in head, especially pressing and bursting pain were produced in both the groups
- Itching of right eye was produced with both placebo and verum by the same prover, also watery discharge from eye was produced in both the groups
- Sneezing and running nose was produced in both the groups
- Pain in abdomen was also exhibited by both groups
- Constipation was produced by verum group alone
- In the extremities, placebo developed trembling of hands and legs only, while verum group developed pressing and aching pain, radiating from elbow to fingers and from knees to toes. The shoulder joints were also affected. There was an affinity toward the right side
- Skin eruptions with itching and burning, aggravated in evening or night and by warmth and ameliorated by cold was developed in verum group alone
- Sleepiness was also overlapping in both the groups, but other characteristics, concomitants or associated complaints were different.

Further, the symptoms mentioned in previous homoeopathic literature<sup>[13-15]</sup> including pathogenetic symptoms of *Mentha piperita* were compared with those produced in this proving. Several similar symptoms emerged and a few symptoms were of opposite nature [Table 3].

Symptoms of *Mentha piperita* already mentioned in text books<sup>[13-17]</sup> like ‘headache in morning,’ ‘sharp pain in left temple,’ ‘pricking pain in throat with difficulty in swallowing and hoarseness of voice,’ ‘bilious colic,’ cough, pain in right

foot, small eruptions with much itching, pruritus vulvae and vesicular eruptions (similar to herpes zoster) reappeared in this proving and can be considered as reproving symptoms.

None of the symptoms developed during the trial were severe to require antidote. Thus, no adverse event was reported in this trial.

The statistical analysis using paired *t*-test for the laboratory investigation parameters at PME and Post-trial Medical Examination (TME) for the provers who developed symptoms in both the groups was carried out. Statistically significant difference found in the eosinophil percentage in verum group and TRBC count in the Placebo group [Table 4].

Statistically significant change in eosinophil percentage ( $P = 0.001$ ) was also found on carrying out paired *t*-test for the laboratory investigation parameters at PME and post-trial medical examination (TME) for all the provers in the verum group [Table 5].

The changes in each laboratory parameter before and after the trial between the groups were analysed using unpaired *t*-test and the groups were found comparable [Table 6].

Apart from these blood examination findings, comparison in the PME and TME for findings in pathological investigations of urine, stool and radiological investigations were done but no significant changes were observed.

## DISCUSSION

In this trial, both the verum and placebo groups were comparable at baseline. The lower potencies have produced a greater number of symptoms, which might indicate that the lower potencies of this drug could be more effective. The number of symptoms produced by females was much higher than the number of symptoms produced by male provers. Thus, the sensitivity or the affinity of this drug seems to be more towards the female gender.

The analysis of the symptoms showed that there was an overlapping of 12 symptoms in both groups. This overlapping of the symptoms in the verum and placebo groups may be due to the nocebo effect<sup>[22]</sup> and as per inter-prover analysis, these have been eliminated from the final pathogenetic symptoms of this drug substance.

Comparison of the laboratory parameters showed statistically significant change in percentage of eosinophils in the verum group; however, it was within normal range, whereas the change was not significant in the placebo group. This could be attributed to the effect of *Mentha piperita* in reducing the allergic reaction in the respiratory system. This needs further validation during clinical verification.

No adverse event or any pathological change beyond the normal range was reported during the trial. Thus, it has substantiated that the drug proving trials do not cause any pathological change.

**Table 2: Pathogenetic symptoms after comparison between symptoms produced in Placebo and Verum groups**

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Mind	Dullness, no desire for any work, does not want to study, <i>agg.</i> after sleep, <i>amel.</i> lying on abdomen	Forgetfulness, <i>agg.</i> evening (unable to recall the studied material)				Forgetfulness, <i>agg.</i> evening (unable to recall the studied material)
Head	<p>Congestive pressing pain in the frontal region of the head, <i>agg.</i> 5 to 8 pm, <i>amel.</i> sleep after. Associated with heaviness of occiput and sleepiness. Headache appeared and disappeared gradually</p> <p>Pressing pain from upper eyelid to occiput associated with heaviness of eyes and unable to open eyes, <i>agg.</i> by rest, <i>amel.</i> by open air, motion, after eating.</p> <p>Bursting pain in forehead, vertex and temporal region with heaviness of head, <i>agg.</i> motion, <i>amel.</i> rest, after sleep, engaged in work (10 am to 5 pm)</p> <p>Dull aching pain in the frontal region of head (12 to 12.15 pm)</p> <p>Sudden severe paroxysmal headache in right temporal region (each paroxysm lasting for 5-10 min) (12.05 to 10 pm, for next 4 days- waking up at 7 am and slept at 10 pm)</p> <p>Heaviness of right side of head with reeling sensation, <i>agg.</i> evening.</p> <p>Pulsating pain in occipital region of head, <i>amel.</i> by rest (2.18 to 2.35 pm)</p> <p>Pressing pain in occipital region of head with <i>agg.</i> heat, 12 to 5 pm, <i>amel.</i> cold application</p> <p>Pulsating pain in occipital region of head, <i>agg.</i> mental exertion, open air, <i>amel.</i> by sleep, closed room</p> <p>Pulsating pain in occipital region of head, starts from occiput and settles over left eye, <i>agg.</i> by movement, morning</p> <p>Bursting pain in frontal region of head, <i>agg.</i> warm, closed room, evening, <i>amel.</i> open air, fresh air. (2.20-4 pm)</p> <p>Throbbing pain in right side of the head, starts from occiput and extends upto the right supraorbital region, <i>agg.</i> night and <i>amel.</i> morning</p> <p>Heaviness of head associated with nausea for few minutes, <i>amel.</i> by rest</p>	<p>Pressing pain all over head with apprehension and increased appetite, <i>agg.</i> morning</p> <p>Pricking pain in left half of head started gradually with restlessness and irritability, <i>agg.</i> warmth, mental exertion, 3.30 to 8.40 pm, <i>amel.</i> rest, cold application</p>	<p>Sudden pressing pain and tightness from parietal to occipital region, <i>agg.</i> morning, night, moving, waking up, <i>amel.</i> evening, rest, sleep after. Associated with heaviness of head and sensation as if head is empty and tiredness</p> <p>Throbbing pain in right frontal region, <i>amel.</i> lying down (1.30 to 1.45 pm).</p> <p>Bursting pain in forehead. <i>agg.</i> movement, <i>amel.</i> pressure.</p> <p>Throbbing pain in right side of forehead just above the eyes, <i>amel.</i> by pressure.</p>	<p>Heaviness in head, <i>amel.</i> pressure, lying on right side, <i>agg.</i> evening. Associated with sleepiness, dryness of mouth, thirstlessness, decreased appetite and weakness</p>	<p>Throbbing pain in B/L temporal region, <i>agg.</i> motion, open air, evening, <i>amel.</i> by rest, closed room (3 pm to 6.30 pm and next day- 3.30 pm to 6 pm)</p> <p>Throbbing pain in B/L temporal region, <i>agg.</i> motion, open air, evening, <i>amel.</i> by rest, closed room (3 pm to 6.30 pm and next day- 3.30 pm to 6 pm)</p> <p>Throbbing pain in right frontal region, <i>amel.</i> lying down (1.30 to 1.45 pm)</p> <p>Throbbing pain in right side of forehead just above the eyes, <i>amel.</i> by pressure.</p> <p>Pressing pain all over head with apprehension and increased appetite, <i>agg.</i> morning.</p> <p>Pricking pain in left half of head started gradually with restlessness and irritability, <i>agg.</i> warmth, mental exertion, 3.30 to 8.40 pm, <i>amel.</i> rest, cold application.</p> <p>Bursting pain in forehead, <i>agg.</i> movement, <i>amel.</i> pressure.</p>	<p>Sudden pressing pain and tightness from parietal to occipital region, <i>agg.</i> morning, night, moving, waking up, <i>amel.</i> evening, rest, sleep after. Associated with heaviness of head and sensation as if head is empty and tiredness</p> <p>Heaviness in head, <i>amel.</i> pressure, lying on right side, <i>agg.</i> evening. Associated with sleepiness, dryness of mouth, thirstlessness, decreased appetite and weakness.</p> <p>Throbbing pain in B/L temporal region, <i>agg.</i> motion, open air, evening, <i>amel.</i> by rest, closed room (3 pm to 6.30 pm and next day- 3.30 pm to 6 pm)</p> <p>Throbbing pain in right frontal region, <i>amel.</i> lying down (1.30 to 1.45 pm)</p> <p>Throbbing pain in right side of forehead just above the eyes, <i>amel.</i> by pressure.</p> <p>Pressing pain all over head with apprehension and increased appetite, <i>agg.</i> morning.</p> <p>Pricking pain in left half of head started gradually with restlessness and irritability, <i>agg.</i> warmth, mental exertion, 3.30 to 8.40 pm, <i>amel.</i> rest, cold application.</p> <p>Bursting pain in forehead, <i>agg.</i> movement, <i>amel.</i> pressure.</p>

(Contd...)

Table 2: (Continued)

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Eye	Itching in right eye Watery discharge from eyes, <i>agg.</i> sunlight, warm room, <i>amel.</i> open air, cold air, sleep after (7–8 am)	Itching in right eye, episode lasting for half an hour, <i>agg.</i> morning Redness and watering of left eye, with sticky white discharge from left eye, <i>agg.</i> morning, <i>amel.</i> cold application. (6–9 am)		Sudden itching, burning sensation in both eyes with sleepiness, <i>amel.</i> sleep after, cold water application. No sleepiness in next 2 days but itching and burning felt more on right side		Itching in right eye, episode lasting for half an hour, <i>agg.</i> morning Sudden itching, burning sensation in both eyes with sleepiness, <i>amel.</i> sleep after, cold water application. No sleepiness in next 2 days but itching and burning felt more on right side Redness and watering of left eye, with sticky white discharge from left eye, <i>agg.</i> morning, <i>amel.</i> cold application (6–9 am)
Ear		Stitching pain in left ear, appeared suddenly and disappeared suddenly (4.30–4.35 pm)				Stitching pain in left ear, appeared suddenly and disappeared suddenly. (4.30–4.35 pm)
Nose	Obstruction of nose, <i>agg.</i> lying down, morning, <i>amel.</i> sitting. (7–8 am) Sneezing and running nose with lachrymation, itching and redness of eyes, more on right side. (10.30–11.10 pm) Sudden, bilateral nasal obstruction with nausea, <i>agg.</i> lying down, <i>amel.</i> blowing the nose. (5–7 am) Sneezing in morning after waking up. (9–11 am)			Obstruction of nose with dyspnoea, <i>agg.</i> night, closed room, <i>amel.</i> washing face with cold water, open air Obstruction of nose with dyspnoea and sore throat, <i>agg.</i> morning, <i>amel.</i> bathing cold water	Sneezing, watery discharge from nose, <i>agg.</i> fanning, cold air, <i>amel.</i> warm room, after sleep. Associated with heaviness of head, weakness, thirstlessness with dry tongue, sleepiness and obstruction of nose. Complaint started suddenly and disappeared slowly. (7 to 10 pm and next day 9–10 am)	Obstruction of nose with dyspnoea, <i>agg.</i> night, closed room, <i>amel.</i> washing face with cold water, open air. Obstruction of nose with dyspnoea and sore throat, <i>agg.</i> morning, <i>amel.</i> bathing cold water Sneezing, watery discharge from nose, <i>agg.</i> fanning, cold air, <i>amel.</i> warm room, after sleep. Associated with heaviness of head, weakness, thirstlessness with dry tongue, sleepiness and obstruction of nose. Complaint started suddenly and disappeared slowly. (7–10 pm and next day 9–10 am)
Face	Small papular red eruptions on face, especially on forehead.  Stiffness with pain in a spot over left jaw. (4–4.15 pm) Shooting pain in right side of jaw extending to the right ear Pain in the right jaw in small portion (spot) just below right ear				Soreness in right maxillary region, <i>agg.</i> bending forward. (2–11 pm next day)	Soreness in right maxillary region, <i>agg.</i> bending forward. (2–11 pm next day)

(Contd...)



**Table 2: (Continued)**

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Mouth	Mild pulsating pain in small portion (spot) of right lower jaw, just below right ear lobe Aphthous ulcer in mouth opposite 1 <sup>st</sup> premolar teeth lower right side with tenderness, burning, cutting pain, <i>amel.</i> warm water gargles Dryness of tongue with increased thirst. (10.30–11.30 am)	Thickly greenish coated tongue must be cleaned 7-8 times and ends with profuse stringy salivation, <i>agg.</i> morning		Aphthae on the right margin of tongue just beside the tip, with burning, <i>agg.</i> after eating salty things		Thickly greenish coated tongue must be cleaned 7–8 times and ends with profuse stringy salivation, <i>agg.</i> morning Aphthae on the right margin of tongue just beside the tip, with burning, <i>agg.</i> after eating salty things
Throat	Dry cough with dryness of throat whole day, <i>agg.</i> evening, <i>amel.</i> drinking water	Hoarseness and pricking pain in throat, <i>agg.</i> swallowing, associated with dry cough			Soreness in throat with difficulty in swallowing	Hoarseness and pricking pain in throat, <i>agg.</i> swallowing, associated with dry cough Soreness in throat with difficulty in swallowing
Stomach	Nausea, <i>agg.</i> after eating	Appetite and thirst decreased throughout the day		Increased thirst for large quantity of water at long interval		Increased thirst for large quantity of water at long interval Appetite and thirst decreased throughout the day
Abdomen	Cramping pain in whole abdomen, more in umbilical region, <i>amel.</i> pressure (11.05–11.20 pm) Sudden stabbing pain in right lower abdomen, <i>amel.</i> sitting. (1–1.10 am) Throbbing pain in left lumbar region. (4.45–4.55 pm)	Cutting pain in left side of lower abdomen, sleep disturbed due to pain. (11 pm–4 am)	Cutting pain with tenderness radiating from umbilicus to hypogastric region, <i>agg.</i> standing, 1 to 4 pm, <i>amel.</i> pressure		Cramping pain in whole abdomen, <i>agg.</i> during stool, <i>amel.</i> after stool. Associated with diarrhoea-watery, scanty with mucous. (3 am to 9.30 am) Mild piercing pain in umbilical region of abdomen, <i>amel.</i> rest, <i>agg.</i> walking. (11.30–11.40 am)	Cutting pain with tenderness radiating from umbilicus to hypogastric region, <i>agg.</i> standing, 1–4 pm, <i>amel.</i> pressure Cramping pain in whole abdomen, <i>agg.</i> during stool, <i>amel.</i> after stool. Associated with diarrhoea-watery, scanty with mucous. (3–9.30 am) Cutting pain in left side of lower abdomen, sleep disturbed due to pain. (11 pm to 4 am) Mild piercing pain in umbilical region of abdomen, <i>amel.</i> rest, <i>agg.</i> walking. (11.30–11.40 am)
Urinary organs	Increased frequency of urination, more in 1 <sup>st</sup> h–6 times in a hour associated with disturbed sleep and restlessness, frequently changing positions	Dragging pain in urethra with scanty urination, <i>agg.</i> exertion, walking, evening, <i>amel.</i> rest, crossing leg, drinking water. Started slowly and disappeared slowly	Urinary organs			Dragging pain in urethra with scanty urination, <i>agg.</i> exertion, walking, evening, <i>amel.</i> rest, crossing leg, drinking water. Started slowly and disappeared slowly

(Contd...)

Table 2: (Continued)

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Rectum			Stool constipated, hard, offensive and black in colour with loss of appetite	Constipation, unsatisfactory soft stool, as if stool stuck at anus, evacuation only by pressure		Constipation, unsatisfactory soft stool, as if stool stuck at anus, evacuation only by pressure Stool constipated, hard, offensive and black in colour with loss of appetite
Male genitalia				Nocturnal emissions with dreams of women whole night. (twice 3 am and 5 am)		Nocturnal emissions with dreams of women whole night. (twice- 3 am and 5 am)
Female Genitalia	Leucorrhoea with nausea, <i>agg.</i> before menses, morning, 7 am Menses- dark brown, scanty, with pain in lower abdomen, lumbar region and right leg	Leucorrhoea with cutting pain in left side of lower abdomen. Leucorrhoea thick, stringy, sticky and ropy, associated with weakness and irritability Pain in lower abdomen and thighs during menses, blood black with small clots. Pain, <i>amel.</i> lying on left side, walking				Leucorrhoea with cutting pain in left side of lower abdomen. Leucorrhoea thick, stringy, sticky and ropy, associated with weakness and irritability Pain in lower abdomen and thighs during menses, blood black with small clots. Pain, <i>amel.</i> lying on left side, walking
Back			Aching pain in lumbar region with soreness and tenderness, <i>agg.</i> lying down on back, afternoon, <i>amel.</i> pressure Drawing pain in nape of neck, <i>amel.</i> lying down		Pricking pain in back extending from left iliac region to left knee, <i>agg.</i> cycling, motion, 7 pm, night, <i>amel.</i> sleep after, lying on painful side, rest	Aching pain in lumbar region with soreness and tenderness, <i>agg.</i> lying down on back, afternoon, <i>amel.</i> pressure Pricking pain in back extending from left iliac region to left knee, <i>agg.</i> cycling, motion, 7 pm, night, <i>amel.</i> sleep after, lying on painful side, rest Drawing pain in nape of neck, <i>amel.</i> lying down
Chest	Heaviness in chest, appeared and disappeared suddenly, <i>agg.</i> afternoon			Cough, <i>agg.</i> midnight, <i>amel.</i> drinking water		Cough, <i>agg.</i> midnight, <i>amel.</i> drinking water

(Contd...)

Table 2: (Continued)

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Extremities	Trembling of both legs started suddenly, <i>agg.</i> Noon, <i>amel.</i> holding with hand Trembling of both hands, more in right than left.	Dull pain with heaviness in both legs, from knee to ankle, <i>agg.</i> walking, <i>amel.</i> rest Small, pointed red eruptions on the front of right arm with itching, <i>amel.</i> itching, cold application, <i>agg.</i> warmth, evening Small, pointed red eruptions on left palm with itching and burning, <i>amel.</i> scratching, cold application, <i>agg.</i> warmth, evening	Trembling in right thumb, <i>agg.</i> writing Pressing pain from elbow to fingers more on right side, <i>agg.</i> right side, with tremor, restlessness and inability to write, <i>amel.</i> by rest. Next day tremor and restlessness from elbow to fingers, <i>amel.</i> by holding with hand Pressing pain from knees to toes more on right side with tremor and restlessness, <i>amel.</i> by rest Aching pain in right leg from knee to ankle, <i>amel.</i> by pressure Pain in right shoulder joint, <i>agg.</i> by raising hand Pain in left shoulder, <i>agg.</i> by raising hand Small vesicular eruptions with itching and burning in left gluteal region for 14 days, <i>agg.</i> night, warmth, <i>amel.</i> cold. On the 10 <sup>th</sup> day, itching and burning in medial side of thigh and popliteal fossa <i>agg.</i> night, which continued for 9 days		Aching pain with stiffness in right knee joint next day same symptom in left knee, <i>amel.</i> pressure, <i>agg.</i> night	Trembling in right thumb, <i>agg.</i> writing Pressing pain from elbow to fingers more on right side, <i>agg.</i> right side, with tremor, restlessness and inability to write, <i>amel.</i> by rest. Next day tremor and restlessness from elbow to fingers, <i>amel.</i> by holding with hand Pressing pain from knees to toes more on right side with tremor and restlessness, <i>amel.</i> by rest Aching pain with stiffness in right knee joint next day same symptom in left knee, <i>amel.</i> pressure, <i>agg.</i> night Dull pain with heaviness in both legs, from knee to ankle, <i>agg.</i> walking, <i>amel.</i> rest Small, pointed red eruptions on the front of right arm with itching, <i>amel.</i> itching, cold application, <i>agg.</i> warmth, evening Small, pointed red eruptions on left palm with itching and burning, <i>amel.</i> scratching, cold application, <i>agg.</i> warmth, evening Aching pain in right leg from knee to ankle, <i>amel.</i> by pressure Pain in right shoulder joint, <i>agg.</i> by raising hand Pain in left shoulder, <i>agg.</i> by raising hand Small vesicular eruptions with itching and burning in left gluteal region for 14 days, <i>agg.</i> night, warmth, <i>amel.</i> cold. On the 10 <sup>th</sup> day, itching and burning in medial side of thigh and popliteal fossa <i>agg.</i> night, which continued for 9 days Bilaterally symmetrical dry black patch on arms (first left then right)

(Contd...)

Table 2: (Continued)

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
Sleep	Drowsiness, <i>agg.</i> evening	Yawning with sleepiness and giddiness, <i>agg.</i> morning, 9.30 am	Sleepiness with desire to lie on left side, bed feels hard. Pain all over the body after getting up, <i>agg.</i> evening Sleeplessness/ Sleep reduced – only for 3–5 h (sleep normal- 11 pm to 8 am)	Sleepiness with weakness and slept for 2–3 h during the day. (normally does not sleep in day) Excessive sleepiness (from 8 pm to 11 pm), Slept from 11pm to 9 am, unable to wake up in next morning Sleepiness with tiredness, slept for 11 h during the night. (9.45 pm, slept at 10 pm (normal sleep- 11.30–7 am) woke at 9 am, weakness continued for 1 h after waking- 9–10 am) (2 <sup>nd</sup> day- slept 10 pm to 9 am) Sleepiness with repetitive yawning associated with redness of eyes. (11.15 am to 12 noon)	Sleepiness from 10 to 10.30 am and slept for 5 h during the day, felt sleepy again in the evening and slept for around 11 h Sleepiness with tiredness (9.30–10 pm) (deep sleep from 10 pm to next day 9 am for 3 days). Weakness for 1 h after waking. (9–10 am). On next day associated with cutting pain in lumbosacral region. (9–10 pm) Deep sleep unable to wake up.(10 pm to 8.30 am, next day- 9.30 pm to 7.30 am) (normal sleep 11 pm to 6.30 am)	Yawning with sleepiness and giddiness, <i>agg.</i> morning, 9.30 am Sleepiness with desire to lie on left side, bed feels hard. Pain all over the body after getting up, <i>agg.</i> evening Sleeplessness/Sleep reduced – only for 3–5 h (sleep normal-11 pm to 8 am) Sleepiness with weakness and slept for 2–3 h during the day. (normally does not sleep in day) Excessive sleepiness (from 8 pm to 11 pm), Slept from 11pm to 9 am, unable to wake up in next morning Sleepiness with tiredness, slept for 11 h during the night. (9.45 pm, slept at 10 pm (normal sleep- 11.30–7 am) woke at 9 am, weakness continued for 1 h after waking- 9–10 am) (2 <sup>nd</sup> day- slept 10 pm to 9 am) Sleepiness with repetitive yawning associated with redness of eyes. (11.15 am to 12 noon) Sleepiness from 10 to 10.30 am and slept for 5 h during the day, felt sleepy again in the evening and slept for around 11 h Sleepiness with tiredness (9.30–10 pm) (deep sleep from 10 pm to next day 9 am for 3 days). Weakness for 1 h after waking. (9–10 am). On next day associated with cutting pain in lumbosacral region. (9–10 pm) Deep sleep unable to wake up.(10 pm to 8.30 am, next day- 9.30 pm to 7.30 am) (normal sleep 11 pm to 6.30 am)

(Contd...)

**Table 2: (Continued)**

Section	Placebo	<i>Mentha piperita</i> 6C	<i>Mentha piperita</i> 12C	<i>Mentha piperita</i> 30C	<i>Mentha piperita</i> 200C	Pathogenetic symptoms after eliminating the common symptoms found both in Verum and placebo group
	<p>Disturbed sleep with mental restlessness, no sleep till 12 midnight and woke up at 2 am and after 1 day, again disturbed sleep with mental restlessness from 12 midnight to 3 am.</p> <p>Sleepiness with yawning, burning sensation in both eyes, <i>agg.</i> morning, <i>amel.</i> sleep.</p> <p>Deep sleep unable to wake up with tiredness. (slept from 11 pm to 9 am)</p> <p>Sleepiness with repetitive yawning. (7–7.50 am) deep sleep during daytime. (8–11 am)</p> <p>Laziness and giddiness, wants to take rest associated with bitter taste in mouth. (2.30–5 pm)</p> <p>Drowsiness with blurred vision, wants to sleep. After 29 days recurrence of same symptom which continued for 7 days</p>					
Fever	<p>Mild fever comes suddenly lasts for 2 h, 9–11 am, great thirst for cold water, no perspiration, no appetite during fever, <i>agg.</i> in warm room, mental exertion, <i>amel.</i> open air, rest, cold application, sleep</p>				<p>Mild fever ranging between 99F and 100F with pain in whole body, thirst increased during fever with dryness of mouth and desire to lie down. (2–6 pm)</p>	<p>Mild fever ranging between 99F to 100F with pain in whole body, thirst increased during fever with dryness of mouth and desire to lie down. (2–6 pm)</p>
Skin	<p>Small boil on right axilla with redness, sensitive to touch <i>agg.</i> pressure. Pus formation on 2<sup>nd</sup> day and discharge of blood and pus on 3<sup>rd</sup> day, pain and redness decrease on 4<sup>th</sup> day and boil decreases and pain absent on the 5<sup>th</sup> day.</p> <p>Dry blackish patch on right arm with no itching</p>		<p>Bilaterally symmetrical dry black patch on arms (first left then right)</p>		<p>Pruritus pubic region then ascends to flank, then to abdomen, back and lastly chest, <i>agg.</i> 10 pm (5.10 pm to after 4 days- 11.15 pm)</p>	<p>Pruritus pubic region then ascends to flank, then to abdomen, back and lastly chest, <i>agg.</i> 10 pm (5 pm - 10 pm and on 4<sup>th</sup> day till 11.15 pm)</p>

This proving of *Mentha piperita* has brought out several valuable symptoms as given under Tables 2 and 3. Many of them are new symptoms; some are old symptoms that have shown newer dimensions and characteristics and some of them are in corroboration with the traditional uses of the drug.<sup>[12-17]</sup> On analysing the symptoms produced in all the groups, the organ affinity of the drug was found toward the locomotor system, gastro-intestinal system, respiratory system, head, eye, ear, skin, urinary system, male and female genitalia, etc.

On comparing and analysing the previous proving symptoms of *Mentha piperita* with the current proving, it was found that several old symptoms have reappeared in this proving, thus verifying the symptoms once again. The symptoms have been analysed and segregated as Grade I and Grade II as per the protocol. The Grade I symptoms and those verified in this trial can be given more weightage in the materia medica. Furthermore, newer characteristics, details and concomitants which have emerged, may be taken up for Clinical verification.

**Table 3: Comparison of symptoms of current proving with existing homoeopathic literature**

Symptoms in existing Homoeopathic literature	Symptoms in Proving conducted by Council
Confusion, has cured mental dullness on rising in the morning <sup>[15]</sup>	Forgetfulness, <i>agg.</i> evening
Headache, beginning in the morning; tension towards both ears, especially the right <sup>[15]</sup>	Sudden pressing pain and tightness from parietal to occipital region, <i>agg.</i> morning, night, moving, waking up, <i>amel.</i> evening, rest, sleep after
Headache from one ear to the other; on returning to bed the pain ceased, but came back when getting up, <i>agg.</i> stooping or turning the head <sup>[15]</sup>	Throbbing pain in bilateral temporal region, <i>agg.</i> motion, open air, evening, <i>amel.</i> by rest, closed room
Very sharp pain in the left temple when writing <sup>[15]</sup>	Pricking pain in left half of head started gradually with restlessness and irritability, <i>agg.</i> warmth, mental exertion, <i>amel.</i> rest, cold application
When writing sharp lancinations extend from left ear to all left teeth <sup>[15]</sup>	Stitching pain in left ear, appeared suddenly and disappeared suddenly
Husky voice from reading aloud. Throat dry and painful on swallowing, as if a pin stuck crosswise in pharynx <sup>[15]</sup>	Hoarseness and pricking pain in throat, <i>agg.</i> swallowing, associated with dry cough
All muscles around neck are painful to touch <sup>[15]</sup>	Soreness in throat with difficulty in swallowing
Infantile colic. Bilious colic with great accumulation of gas <sup>[16]</sup>	Drawing pain in nape of neck, <i>amel.</i> lying down
Liability of the skin to inflammation; every scratch becomes a sore. Pimple, with much itching, near left ear, with heat of the part; in the evening <sup>[15]</sup>	Cramping pain in whole abdomen, <i>agg.</i> during stool, <i>amel.</i> after stool. Associated with diarrhoea- watery, scanty with mucous
Vaginal pruritus <sup>[16]</sup>	Cutting pain in left side of lower abdomen, sleep disturbed due to pain
Herpes zoster <sup>[16]</sup>	Small, pointed red eruptions on the front of right arm with itching, <i>amel.</i> itching, cold application, <i>agg.</i> warmth, evening
Opposite Symptoms	Pruritus pubic region then ascends to flank, then to abdomen, back and lastly chest
Sleep good, refreshing and quiet; waking early in morning <sup>[15]</sup>	Small vesicular eruptions with itching and burning in left gluteal region, <i>agg.</i> night, warmth, <i>amel.</i> cold. On 10 <sup>th</sup> day, itching and burning in medial side of thigh and popliteal fossa <i>agg.</i> night
The least feeling of cold excites a cough <sup>[15]</sup>	Excessive sleepiness, unable to wake up in the morning
	Eye, nose, head and skin symptoms <i>ameliorated</i> by cold application

This trial has produced ‘pain in abdomen’ and respiratory symptoms in several provers, thus corroborating with the clinical use of *Mentha piperita* in treating abdominal pain, nausea, irritable bowel syndrome and symptomatic relief of cough and cold. The following symptoms can be correlated with the traditional uses of the drug by corroborating the pathogenetic effects produced in this trial: <sup>[13,14]</sup> Obstruction of nose with dyspnoea; soreness of throat associated with difficulty in swallowing, hoarseness and dry cough; cramping pain in abdomen, aggravated during stool, ameliorated after stool, associated with diarrhoea- watery, scanty with mucous; cutting pain with tenderness radiating from umbilicus to hypogastric region, aggravated by standing and ameliorated by pressure; pain in lower abdomen and thighs during menses. This correlation shows that this trial has produced symptoms corroborating with all the above historical uses of the drug; hence, in a way, it has further established the law of similar.

This study, being a multi-centric trial, was conducted at three different parts of the country, namely, Gudivada, Bhubaneswar and Lucknow. Hence, it was possible to incorporate provers from different geographic and climatic conditions into one trial, in order to get a diverse range of provers. Furthermore, a good number of the symptoms were produced which indicates that the provers were susceptible and sensitive for this drug substance. The appearance of many similar symptoms with respect to the previous proving and traditional use, origin

**Table 4: Analysis of laboratory parameters between PME and TME for provers of both groups who developed symptoms**

Laboratory parameters	Provers with symptoms in Verum group (n=22)			Provers with symptoms in Placebo group (n=7)		
	PME	TME	p value	PME	TME	p value
TRBC	4.27	4.10	0.09	4.71	4.23	0.04
Hb%	12.39	12.16	0.22	13.41	12.37	0.13
TWBC	7600.00	7912.73	0.34	7200.00	7585.71	0.51
DC.N	56.55	59.86	0.14	55.29	60.43	0.27
DC.E	4.77	3.41	0.01	4.29	2.71	0.10
DC.L	37.50	35.36	0.25	39.71	36.14	0.48
ESR	11.59	11.50	0.95	14.57	12.57	0.54
RBS	79.33	82.09	0.30	77.49	79.43	0.63
T. Cholesterol	164.37	162.74	0.65	188.50	182.77	0.42
Urea	20.83	22.93	0.12	23.42	24.11	0.59

TRBC: Total red blood cells, DC.N: Differential count neutrophils, DC.E: Differential count eosinophils, DC.L: Differential count lymphocytes, ESR: Erythrocyte sedimentation rate, T. Cholesterol: Total cholesterol, TWBC: Total white blood cell count

of new characteristic symptoms and specific modalities like amelioration from cold are the major strengths of this study.

Since most of the provers are from the homoeopathic medical colleges, there was dearth of middle and elderly age group on whom the proving could be conducted. Lack of clear cut modalities in many symptoms attribute to the limitations in this study. Considering this, it is suggested that a larger sample size

**Table 5: Analysis of laboratory parameters between PME and TME for verum group (n=32)**

Laboratory parameters	PME	TME	p value
TRBC	4.205±0.456	4.088±0.491	0.142
Hb%	12.359±1.404	12.155±1.424	0.137
TWBC	7589.063±1256.963	7821.250±1239.927	0.372
DC.N	58.031±9.885	61.219±7.889	0.057
DC.E	5.250±2.095	3.531±1.646	0.001
DC.L	35.781±8.746	34.156±8.017	0.260
ESR	11.467±5.444	11.281±6.717	0.627
RBS	79.919±11.442	83.041±13.185	0.202
T. Cholesterol	167.032±27.967	164.693±21.844	0.878
Urea	21.250±5.314	23.650±4.901	0.018

TRBC: Total red blood cells, DC.N: Differential count neutrophils, DC.E: Differential count eosinophils, DC.L: Differential count lymphocytes, ESR: Erythrocyte sedimentation rate, T. Cholesterol: Total cholesterol, TWBC: Total white blood cell count

**Table 6: Analysis of the change in laboratory parameters from PME to TME in verum group with placebo group**

Variable	Change in Verum Group	Change in Placebo Group	p value
SBP	-2.063±6.652	-1.214±6.002	0.673
DBP	0.313±5.591	-0.143±5.112	0.789
TRBC	-0.117±0.438	-0.399±0.413	0.053
Hb%	-0.205±0.759	-0.557±1.392	0.386
TWBC	232.188±1448.467	257.143±1192.099	0.952
DC.N	3.188±9.138	4.286±9.458	0.717
DC.E	-1.719±2.174	-0.643±2.620	0.192
DC.L	-1.625±8.015	-3.429±9.764	0.550
ESR	-0.625±7.201	-0.571±9.858	0.986
RBS	2.568±11.326	2.760±8.442	0.950
T. Cholesterol	0.372±13.413	0.614±7.741	0.939
Urea	1.247±2.857	1.779±8.318	0.819

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TRBC: Total red blood cells, DC.N: Differential count neutrophils, DC.E: Differential count eosinophils, DC.L: Differential count lymphocytes, ESR: Erythrocyte sedimentation rate, T. Cholesterol: Total cholesterol, TWBC: Total white blood cell count

and inclusion of older age groups as subjects could improve the prospects of future reproving of *Mentha piperita*.

## CONCLUSION

Grade I pathogenetic symptoms and the symptoms elicited during this trial were found similar to those in the previous literature of *Mentha piperita*, thus further enriching its Materia Medica. There were new symptoms in the trial, two of which showed opposite character when compared to the previous literature. The statistically significant difference in Differential Eosinophil Count found in the verum group pre-post intervention need to be clinically verified under the clinical verification program of the Council. This will help to further expand the scope of the clinical use of the drug.

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## CONFLICTS OF INTEREST

None declared.

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## Essai pathogénique homéopathique de *Mentha piperita* L.: Un essai multicentrique, en double aveugle, randomisé et contrôlé par placebo

**RÉSUMÉ Introduction:** *Mentha piperita* L, un médicament moins connu et partiellement éprouvé en homéopathie, est largement utilisé en phytothérapie. Objectif: L'objectif de cette étude est d'obtenir la réponse pathogénique de *Mentha piperita* en comparaison avec un placebo. **Matériaux et méthodes:** Un essai clinique multicentrique, en double aveugle, contrôlé par placebo et randomisé a été réalisé dans trois centres auprès de 46 sujets relativement sains. Après randomisation, 32 sujets ont reçu du verum en 6C, 12C, 30C et 200C et, dans le groupe placebo, 14 sujets ont reçu des globules identiques non médicamentés. Tous les changements ont été enregistrés par les prescripteurs et élaborés par les maîtres de stage. Les données ont finalement été traitées dans la cellule de traitement des données. **Résultats:** Sur les 32 testeurs du groupe Verum, 22 ont rapporté 61 symptômes, alors que 24 symptômes ont été rapportés par sept testeurs du groupe placebo. La majorité des symptômes ont été produits dans le domaine de l'appareil locomoteur, suivi par l'appareil gastro-intestinal et d'autres appareils. Au total, dix nouveaux symptômes de grade I ont été identifiés, tandis que 11 symptômes étaient similaires à ceux trouvés dans la littérature antérieure. **Conclusion:** *Mentha piperita* a révélé une réponse pathogène significative dans cet essai, ce qui confirme son utilisation traditionnelle et les symptômes observés précédemment. Parmi les symptômes nouvellement développés, deux symptômes qui ont montré un caractère opposé par rapport à la littérature précédente, et la différence statistiquement significative trouvée dans la numération différentielle des éosinophiles dans le groupe verum après l'intervention sont les résultats qui doivent être vérifiés cliniquement pour améliorer la portée de leur utilisation clinique.

## Homöopathische pathogenetische Prüfung von *Mentha piperita* L.: Eine multizentrische, doppelblinde, randomisierte und placebokontrollierte Studie

**Abstrakt Einführung:** *Mentha piperita* L, ein in der Homöopathie weniger bekanntes und teilweise bewährtes Arzneimittel, wird in großem Umfang als pflanzliches Arzneimittel verwendet. **Zielsetzung:** Ziel dieser Studie ist es, die pathogenetische Reaktion von *Mentha piperita* im Vergleich zu Placebo zu ermitteln. **Materialien und Methoden:** Eine multizentrische, doppelblinde, placebokontrollierte und randomisierte klinische Studie wurde an drei Zentren mit 46 relativ gesunden Probanden durchgeführt. Nach der Randomisierung erhielten 32 Probanden Verum in den Potenzen 6C, 12C, 30C und 200C, während in der Placebogruppe 14 Probanden identische, unarzneiliche Globuli verabreicht wurden. Alle Änderungen wurden von den Prüfern aufgezeichnet und von Prüfmeistern ausgearbeitet. Die Daten wurden schließlich in der Prüf- und Datenverarbeitungszelle verarbeitet. **Ergebnisse:** Von den 32 Probanden der Verumgruppe berichteten 22 über 61 Symptome, während sieben Probanden der Placebogruppe 24 Symptome angaben. Die meisten Symptome traten im Bereich des Bewegungsapparates auf, gefolgt vom Magen-Darm-Trakt und anderen Systemen. Insgesamt wurden zehn neue Symptome des Grades I identifiziert, während 11 Symptome denen ähnelten, die in der bisherigen Literatur gefunden wurden. **Schlussfolgerung:** *Mentha piperita* zeigte in dieser Studie eine signifikante pathogenetische Reaktion, was seine traditionelle Verwendung und die zuvor beobachteten Symptome bestätigt. Unter den neu entwickelten Symptomen waren zwei Symptome, die im Vergleich zur bisherigen Literatur einen entgegengesetzten Charakter aufwiesen, und ein statistisch signifikanter Unterschied in der differenziellen Eosinophilenzahl in der Verumgruppe nach der Intervention sind die Ergebnisse, die klinisch verifiziert werden müssen, um den Umfang ihrer klinischen Anwendung zu erweitern.

**मेंथा पिपेरिता एल के होम्योपैथिक पैथोजेनेटिक परीक्षण :** एक बहु-केंद्रित, डबल-ब्लाइंड, यादृच्छिक और प्लेसबो-नियंत्रित परीक्षणपरिचय: मेंथा पिपेरिता एल, होम्योपैथी में एक कम ज्ञात और आंशिक रूप से साबित दवा, एक हर्बल दवा के रूप में बड़े पैमाने पर उपयोग की जाती है। **उद्देश्य:** इस अध्ययन का उद्देश्य प्लेसबो की तुलना में मेंथा पिपेरिता की पैथोजेनेटिक प्रतिक्रिया को प्राप्त करना है। **सामग्री और तरीके:** एक बहु-केंद्र, डबल-ब्लाइंड, प्लेसबो-नियंत्रित और यादृच्छिक नैदानिक परीक्षण 46 अपेक्षाकृत स्वस्थ प्रोवर्स के साथ तीन केंद्रों पर किया गया था। यादृच्छिक करण के बाद, 32 प्रोवर्स को 6सी, 12सी, 30सी और 200 शक्ति में वेरम दिया गया था और प्लासबो समूह में, 14 प्रोवर्स को समान, अचिकित्सकीय ग्लोबिडल गोलियाँ दिया गया था। सभी परिवर्तनों को प्रोवर्स द्वारा दर्ज किया गया था और प्रोविंग मास्टर द्वारा साबित करके विस्तृत किया गया था। डेटा को अंततः साबित-सह-डेटा प्रोसेसिंग सेल में संसाधित किया गया था। **परिणाम:** वेरम समूह के 32 प्रोवर्स में से, 22 ने 61 लक्षणों की सूचना दी, जबकि प्लेसबो समूह में सात प्रोवर्स द्वारा 24 लक्षणों की सूचना दी गई थी। अधिकांश लक्षण लोकोमोटर सिस्टम के क्षेत्र में उत्पादित किए गए थे, इसके बाद अन्य प्रणालियों के बगल में गैस्ट्रो-आंत्र प्रणाली में थे। कुल मिलाकर, दस नए ग्रेड I लक्षणों की पहचान की गई थी, जबकि 11 लक्षण पिछले साहित्यिक सामग्री में पाए गए लोगों के समान थे। **निष्कर्ष:** मेंथा पिपेरिता ने इस परीक्षण में एक महत्वपूर्ण पैथोजेनेटिक प्रतिक्रिया का खुलासा किया जो इसके पारंपरिक उपयोग की पुष्टि करता है और पहले देखे गए लक्षणों की पुष्टि करता है। नए विकसित लक्षणों में से, पिछले साहित्य की तुलना में दिखाए गए दो लक्षणों ने विपरीत चरित्र दिखाया है, और वेरम समूह में विभेदक ईसिनोफिल गिनती में पाए जाने वाले सांख्यिकीय रूप से महत्वपूर्ण अंतर-हस्तक्षेप के बाद के निष्कर्ष हैं जिन्हें उनके नैदानिक उपयोग के दायरे को बढ़ाने के लिए नैदानिक रूप से सत्यापित करने की आवश्यकता है।

## Ensayo patogenético homeopático de *Mentha piperita* L.: Un ensayo multicéntrico, doble ciego, aleatorizado y controlado con placebo

**Abstracto la introducción:** *Mentha piperita* L, una droga menos conocida y parcialmente probada en homeopatía, se usa extensivamente como medicina herbaria. **Objetivo:** El objetivo de este estudio es obtener la respuesta patogenética de *Mentha piperita* en comparación con el placebo. **Materiales y métodos:** Se llevó a cabo un ensayo clínico multicéntrico, doble ciego, controlado con placebo y aleatorizado en tres centros con 46 probadores relativamente sanos. Después de la aleatorización, 32 probadores recibieron verum en potencias de 6C, 12C, 30C y 200C y en el grupo placebo, se administraron 14 probadores de glóbulos idénticos no medicados. Todos los cambios fueron registrados por los probadores y elaborados por maestros de prueba. Los datos se procesaron finalmente en la celda de procesamiento de pruebas. **Resultados:** De los 32 probados del grupo Verum, 22 informaron 61 síntomas, mientras que 24 síntomas fueron reportados por siete probados en el grupo placebo. La mayoría de los síntomas se produjeron en la esfera del aparato locomotor, seguido del sistema gastrointestinal junto a otros sistemas. En total, se identificaron diez nuevos síntomas de grado I, mientras que 11 síntomas fueron similares a los encontrados en la literatura anterior. **Conclusión:** *Mentha piperita* reveló una respuesta patogenética significativa en este ensayo que verifica su uso tradicional y síntomas previamente observados. Entre los síntomas recién desarrollados, dos síntomas que mostraron un carácter opuesto en comparación con la literatura anterior, y una diferencia estadísticamente significativa encontrada en el recuento diferencial de eosinófilos en el grupo verum post-intervención, son los hallazgos que necesitan ser verificados clínicamente para mejorar el alcance de su uso clínico.

薄荷属植物的同源性病理试验.: 一项多中心、双盲、随机和安慰剂对照的试验

摘要 简介: 薄荷 (*Mentha piperita* L) 是一种不太知名的、在顺势疗法中被部分证实的药物, 被广泛地用作草药。目标: 本研究的目的是在与安慰剂的比较中激发薄荷的致病反应。材料和方法: 在三个中心进行了一项多中心、双盲、安慰剂对照和随机的临床试验, 有46名相对健康的证明人参加。随机化后, 32名证明人被给予6C、12C、30C和200C效力的药丸, 在安慰剂组中, 14名证明人被给予相同的、未用药的球状物。所有的变化都由证明人记录, 并由证明人详细说明。数据最终在证明兼数据处理单元进行处理。结果: 在真的组的32名证明人中, 22人报告了61个症状, 而安慰剂组的7名证明人报告了24个症状。大多数症状是在运动系统领域产生的, 其次是胃肠系统和其他系统。总共发现了10个新的I级症状, 而11个症状与以前文献中发现的症状相似。总结: 薄荷在本试验中显示了显著的致病反应, 这验证了其传统用途和以前观察到的症状。在新出现的症状中, 有两个症状与以前的文献相比显示出相反的特征, 而且在干预后的真的组中发现嗜酸性粒细胞计数有统计学上的显著差异, 这些发现需要进行临床验证以提高其临床使用范围。