# FORMULATION AND EVALUATION OF PEPPERMINT OILS AS AN ANTISPASMODIC AGENT: A NOVEL APPROACH TO ALLEVIATING MENSTRUAL CRAMPS

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**ABSTRACT:** Menstrual cramps or dysmenorrhea are a common gynaecological condition experienced by individuals during their reproductive years. Peppermint oil's active ingredient Menthol, is known to relax the smooth muscles of the uterus and temporarily relieves pain by desensitizing pain receptors. The study measured outcomes based on self-reported pain levels, duration of pain, and reliance on conventional pain modifications. This study aims to evaluate the antispasmodic effects of peppermint oils on menstrual cramps, offering a natural alternative for pain relief. Peppermint oil due to its natural antispasmodic properties, appears to be an effective, alternative treatment for reducing the severity of menstrual cramps. Its ease of application and absence of significant side effects make it a viable option for individuals seeking relief from dysmenorrhea. Further studies with larger sample sizes and varying concentrations of peppermint oil are recommended to fully understand its benefits and potential applications in gynaecological practices.

**KEYWORDS:** Primary Dysmenorrhea, peppermint oil, Mentha Piperita, Analgesic, Smooth muscle

## INTRODUCTION:

Menstrual cramp is the occurrence of labour-like pain in the lower abdomen, accompanied by symptoms like nausea, vomiting, diarrhoea, headache and dizziness.[1] Symptoms like as cramps, tiredness, backache, swelling abdomen, and painful breasts have also been described in women with menstrual misery. Menstrual distress has been shown to impair women's daily activities, as well as their reproductive and psychological health, according to research. Menstrual periods are frequently accompanied by a variety of unpleasant symptoms, such as premenstrual syndrome, which includes symptoms such as mild cramping and exhaustion.[2] Dysmenorrhea (period pain) is common and affects around three quarters of all young women under the age of 25. The majority of young women, for a variety of reasons, think of period pain as 'normal' and something to be managed or endured.[3] Dysmenorrhea is one of the most prevalent causes of undesirable effect on women's lives, and sometimes produces activity restriction.[4] Dysmenorrhea is mainly classified into two types; primary and secondary. Primary dysmenorrhea is defined as painful menstruation with cramps in the pelvic area that mostly goes along with other symptoms, like nausea, vomiting, diarrhoea, sweating, and shivering.[5] Primary dysmenorrhea or is a pain associated with menstruation without proven pelvic disease and involves approximately 50 -90% of women with regular menstrual periods.[6]Ten percent of women suffer from severe and debilitating pain for three days which brings limitations in daily activities and social function, and even absence from school and work. For the management of primary dysmenorrhea, various methods have been proposed, including the use of non -steroidal anti- inflammatory drugs [7], contraceptive pills [8], and non -pharmacological methods such as herbal medicines [9] and acupuncture.[10] Due to these reasons, as well as the possible complications of the use of pharmaceutical methods, non-pharmacological treatments for primary dysmenorrhea, such as patient explanation and assertion, behavioural interventions, acupressure, muscle relaxation, music therapy, guided imaging and psychometric methods, cognitive psychotherapy, the use of local heat, yoga, physiotherapy, and Trans Cutaneous Electrical Nerve Stimulation (TEN S) to reduce menstrual pain.[11]

Peppermint herbal products are usually used in treating diseases. Peppermint is one among several plants used in traditional medicine. This plant exerts its effect on the myometrium contractile activity by inhibiting prostaglandin F2α and oxytocin. Menthol is the most important active material in mint. The most important effect

of this treatment is on vomiting and diarrhoea. Furthermore, peppermint extract is identified to have analgesic effect and anti-inflammatory activity. Due to probability of positive effects of peppermint in the treatment of dysmenorrhea against the effects of NSAIDs such as Mefenamic Acid. To compare the effects of herbal medicines to treat primary dysmenorrhea rather than medical drugs we have done this research.[12]

Mints are powerful in decreasing muscle torment, muscle unwinding, and lesson weariness. Mints is a seasoning that is tremendous for its meditational properties, pain relieving, calming, antispasmodic, decongestants, and cell reinforcement impacts. M. Piperita is one of the Mentha animal types (i.e., M. Piperita, Mentha arvensis, and corn mint oil). M. piperita includes menthol and menthone as its real parts. Outer utilization of mint concentrate brought the agony edge up in human. Peppermint fragrance was likewise viable on seen physical remaining burden, the transient outstanding task at hand, exertion, and uneasiness. Gastrointestinal muscles are made to soothe using M. piperita as it relaxes the muscle by the reduction influx of calcium ion concentration in the jejunum and large intestine.[13]

Fennel (Foeniculum vulgare Mill) is one of the oldest spice plants which, due to its economic importance and significant pharmaceutical industry application, is considered as one of the world's most important medicinal plants. F. vulgare commonly called fennel is a perennial herb and flowering plant with feathery leaves and yellow flowers, used in traditional medicine for many ailments. It is one of the oldest medicinal plants in the world. It has many pharmacological properties like anti-inflammatory, anti-bacterial anti-spasmodic, apoptotic, galactagogue, emmenagogue, antioxidant, antifungal, antimicrobial, and memory enhancing property. It has been established that fennel oil will possess a significant antispasmodic or relaxant effect. The essential oil has beneficial effects on primary dysmenorrhea, and it reduce the pain.[14]

Ginger is known to have outweighing benefits among many conventional remedies. It is useful in minimizing menstrual cramps, and it relaxes the muscular spasms as well. It is considered as an anti-inflammatory agent in folk remedies. It also contains non-volatile components like gingerols, shogaols, zingerone, and paradol. Furthermore, it has pleiotropic pharmacological activities, like antioxidants, under the prolonged exposure of the desensitized TRPV1 agonists, capsaicin, which ends in pain relief. Although these herbal medicines were routinely use to treat spasm.[15]

## AIMS AND OBJECTIVES:

Aims: The aim of using peppermint oil as an antispasmodic for menstrual cramps is to alleviate pain and discomfort associated with muscle spasms in the uterus during menstruation. Peppermint oil contain menthol, which has a natural muscle- relaxing effect, help in to reduce the intensity and duration of menstrual cramps when applied topically. Its antispasmodic properties aim to provide relief from painful contractions of the uterine muscle, promoting comfort and well-being during menstruation.

Objectives: The objectives of using peppermint oil as an antispasmodic for menstrual cramps typically include:

1] Muscle relaxation

2] Pain relief

3] Improved comfort

4] Non – invasive treatment [Natural or Traditional treatment]

5] Enhance quality of life.

## MATERIALS AND METHODS:

### Materials:

Herbal Drugs:

1] Peppermint: Local market, Shrirampur

2] Fennel: Local market, Shrirampur

3] Ginger: Local market, Shrirampur

**Chemicals:**

Olive oil, hexane, – Chemical store of Shivajirao Pawar College of Pharmacy, Pachegaon, Newasa.

**Instruments:**

Analytical weighing balance, gas chromatography- mass spectrometer – Shivajirao Pawar College of pharmacy, Pachegaon, Newasa.

**Glassware:**

Beaker, stirrer, measuring cylinder, iodine flask, Soxhlet apparatus, muslin cloth, etc.

**EXPERIMENTAL METHODOLOGY –**

Antispasmodic Peppermint oil can be prepared by using following two methods:

1] Steam Distillation -

Steam distillation is one of the most popular ways will be used to extract essential oils from plants, leaves and flowers. During steam distillation process, 100 g of the peppermint leaves was being placed in the chamber of the essential oil distillation still, and steam passed through the taken sample. When the steam passed through the given sample it picked up the oils and moved into another chamber where it is cooled and condensed. Then, essential oil was separated from the water and bottled for used.

2] Soxhlet extraction:

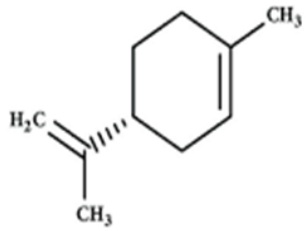
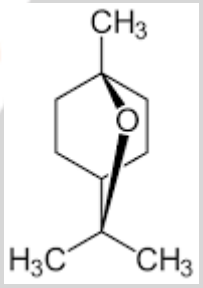
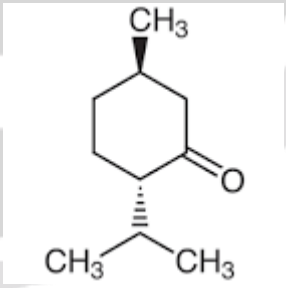
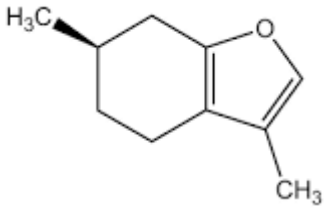
100g of fresh and dry peppermint were weighted and put in Soxhlet apparatus 300 mL of hexane solvent were added. The solvent was heated to reflux then vapour travels up a distillation arm and floods into the chamber housing the thimble of solid. The condenser ensures that any solvent vapour cools, and drips back down into the chamber housing the solid material. The chamber containing
the solid material slowly was filled with warm solvent. Some of the desired compound dissolves in the warm solvent. When the Soxhlet chamber was almost full, the chamber was emptied by the siphon. The solvent was returned to the distillation flask. The thimble ensures that the rapid motion of the solvent does not transport any solid material to the still pot. This cycle was allowed to repeat many times, over hours or days. During each cycle, a portion of the non-volatile compound dissolves in the solvent. After many cycles, the desired compound was concentrated in the distillation flask. The advantage of this system was that instead of many portions of warm solvent being passed through the sample, just one batch of solvent was recycled. After extraction the solvent was removed, typically by means of a rotary evaporator, yielding the extracted oil. The non-soluble portion of the extracted solid remains in the thimble, and is usually discarded.
Simultaneously perform the extraction of fennel and ginger as that of the peppermint leaves.

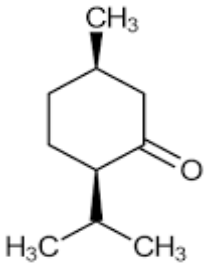
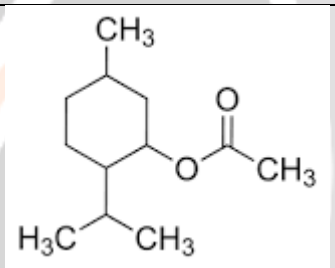
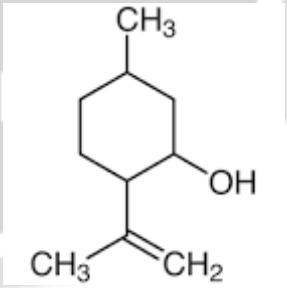
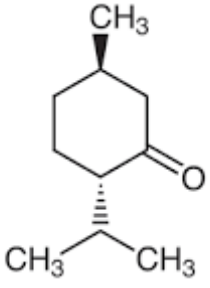
3] General method:

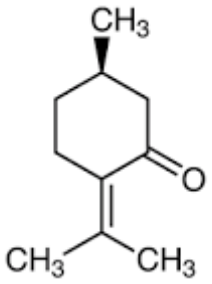
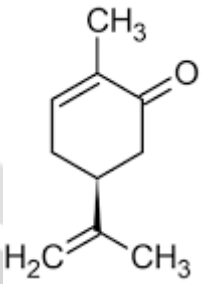
- Crush dry peppermint leaves, fennel, and ginger in a glass jar with a tight lid.
- Cover all the material with olive or grapeseed oil. Close the jar and shake.
- Store for three days. Strain into a bowl and discard the leaves.
- Pack the jar with fresh leaves, pour the oil back in the jar and cover with fresh oil. Repeat until you have the desired amount. Twenty drops of the oil should be diluted with 1.5 ounces of another oil — coconut

or almond, for example — before using it topically, and with water (1 cup per five to 10 drops of oil) for mouthwash. Never put essential oils directly on your skin.

Chemical Constituents: Various constituents of peppermint oil as per monographs of International Pharmacopoeia are limonene (1.0-5.0%), cineole (3.5-14.0%), menthone(14.0-32.0%), menthofuran (1.0-9.0%), isomenthone (1.5-10.0%),methyl acetate (2.8-10.0%), isopulegol (max.0.2%), menthol (30.0-55.0%), pulegone (max.4.0%), and carvone (max.1.0%). The ratio of cineole content to limonene content should be minimum two. Chemical structures of these constituents were given below.

| | | |
|---|---|---|
| 1. | Limonene |  |
| 2. | Cineole |  |
| 3. | Menthone |  |
| 4. | Menthofuran |  |

| | | |
|---|---|---|
| 5. | Isomenthone |  |
| 6. | Menthyl acetate |  |
| 7. | Isopulegol |  |
| 8. | Menthone |  |

| | | |
|---|---|---|
| 9. | Pulegone |  |
| 10. | Carvone |  |

**Evaluation of essential (peppermint) oil:**

- General appearance - A colourless, pale yellow or pale greenish-yellow liquid.
- Organoleptic properties:
- Odour - Characteristic, penetrating
- Taste - Characteristic, pungent, followed by a sensation of cold.
- Acid value - not more than 1.5, determined on 5.0g diluted in 50ml of the prescribed mixture of the solvents.
- Relative density - 0.900-0.916
- Reflective Index - 1.457-1.467
- Optical rotation - -10° to-30°
- Fatty oils and resinified essential oil - complies with the test for fatty oils and resinified essential oils.
- Solvent solubility - Miscible with ethanol (96%), ether and methylene chloride.
- General identity tests - Thin -layer and gas chromatography for characteristic monoterpene profiles.

- Chemical assays: The monoterpene content determined by gas chromatography should be 1,8-cineole (6–14%), limonene (1–5%), menthone (14–32%), menthofuran (1–9%), isomenthone (2–10%), methyl acetate (3–5%), menthol (30–55%), pulegone (not more than 4.0%) and carvone (not more than 1.0%). The ratio of 1, 8-cineole to limonene should be greater than 2.0.[16]

- Chromatography - (2.5–3.5%) and Support-coated open-tubular (SCOT) glass capillary column (43 m x 0.5mm I.D.) coated with SP-1000 was fitted into an aluminium support cage. A Packard-Becker 419 gas chromatograph equipped with dual flame ionization detectors and dual injectors was used. The injection port temperature was 190°C and detector temperature 190°C. The multilinear temperature programmer was used as follows. Initial temperature of 64°C was held for 3 min, then the temperature was raised at 0.5ºC/min to 80ºC, then at 5ºC/min to the final temperature of 155ºC, with an isothermal hold of 12 min at 155°C. The carrier gas was helium at a flow-rate of cu. 2 ml/mm with nitrogen (18 ml/min) as make-up gas. Air flow was 300 ml/min and hydrogen flow 30 ml/min. The velocity of the carrier gas was about 21.5 cm/sec whilst the capacity ratio (k) of the column was 6.5 using docosane at 185C

- Dosage: For External Application, some drops rubbed in the affected areas In semi-solid and oily preparations 5-20 %

- Storage: Store in well-filled, tightly-closed, light-resistant containers in cool place.

- Precautions:

- Peppermint oil is non-toxic and non-irritant in low Dilutions, but sensitization may be a problem due to the Menthol content. It can cause irritation to the skin and Mucus membranes and should be kept well away from the eyes. It should be avoided during pregnancy and should not be used on children under seven. Peppermint oil in any form is not recommended for those with hiatal hernia, gallbladder disease or while pregnant or nursing.

- Overdose symptoms of peppermint oil are slow Breathing, Rapid breathing, Abdominal pain, Diarrhoea, Nausea, Vomiting, Blood in urine, No urine production, Convulsions, Depression, Dizziness, Twitching, Unconsciousness, Uncoordinated movement and Flushing.



**RESULT AND DISCUSSION:**

Result:
Studies evaluating the antispasmodic activity of peppermint oil for relieving menstrual cramps have shown promising results. Peppermint oil contains menthol, which is believed to have muscle-relaxing properties. Research suggests that applying diluted peppermint oil topically or ingesting it orally may help alleviate menstrual cramps by reducing uterine contractions and easing pain. However, more clinical trials are needed to confirm its effectiveness and optimal dosage.

Evaluation of antispasmodic activity:

Drug response relationship observations of Acetylcholine, Peppermint oil, and Atropine

| Drug | Dose | Percentage Response |
|---|---|---|
| Acetylcholine | 0.1 | 68.5% |
| | 0.2 | 85.93% |
| | 0.4 | 93.75% |
| | 0.8 | 100% |
| Atropine +Acetylcholine | 0.1+ 0.1 | 22.22% |
| | 0.1+ 0.2 | 33.33% |
| | 0.1+ 0.4 | 44.44% |
| | 0.1+ 0.8 | 55.55% |
| Peppermint oil + Acetylcholine | 0.1+ 0.1 | 18.75% |
| | 0.1+ 0.2 | 17.18% |
| | 0.1+ 0.4 | 12.5% |

| | | |
|---|---|---|
| | 0.1+ 0.8 | 9.3% |

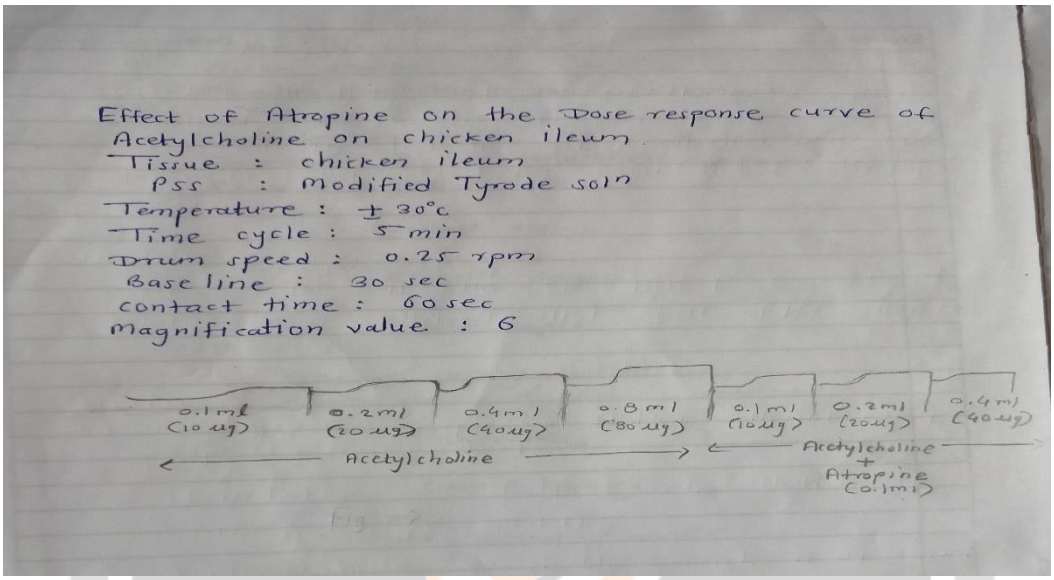



**Fig 1. Dose response curve on Ach and Atropine**

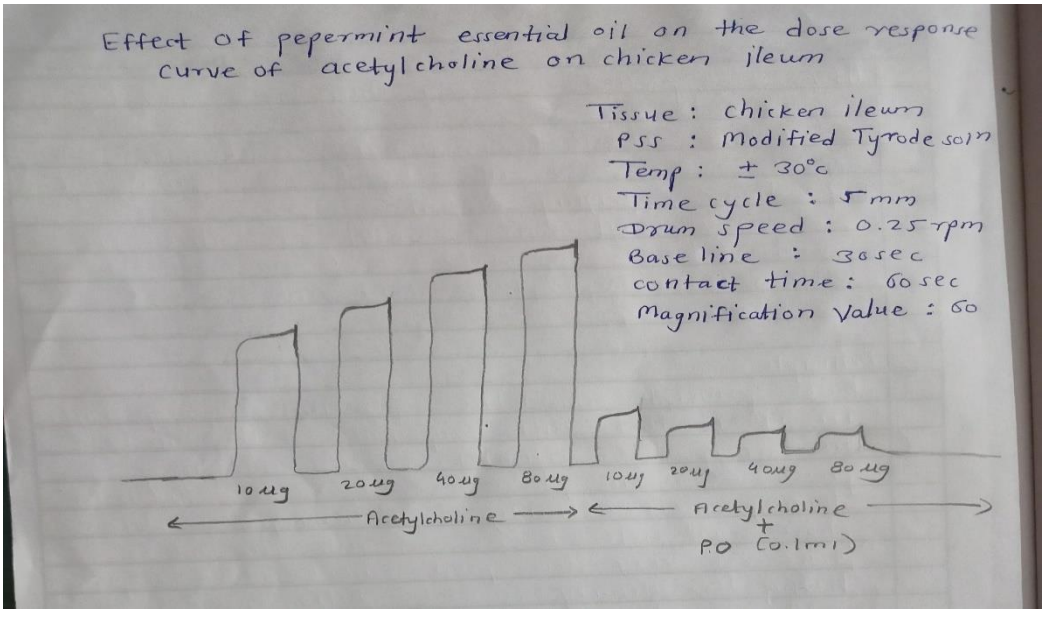



**Fig 2. Dose response curve on Ach + Peppermint oil**

**DISCUSSION:**

For screening the activity of a drug on intestinal smooth muscles, chicken ileum preparations can be used. Chicken intestine is easier to acquire, handle and easier to dissect and has the same reactions to spasmogenic and spasmolytic drugs. Cholinergic agonists like acetylcholine elicit a contractile response in isolated chicken ileum [(17)]. M3receptor, a subtype of cholinergic(muscarinic) receptor activation causes contraction of intestinal smooth muscle.The M3 receptor function through Gq protein and trigger membrane bound phospholipase C (PLc) provoking inositol triphosphate (IP3) and diacylglycerol (DAG) which in succession release Ca2+intracellularly leads to actin-myosin phosphorylation causing increased smooth muscle tone. Thus, the contraction of intestinal smooth muscle in vitro has often been utilized for the study of contractile/dilator responses of agonists as well as antagonist. In current investigation, acetylcholine showed greater contraction while peppermint oil significantly inhibited the acetylcholine induced contraction on isolated chicken ileum preparation. The parallel shift of graph towards right side in acetylcholine dose response curves in the presence of increasing concentrations of PO indicating that there was competitive antagonism between acetylcholine and PO for M3-receptors present on the smooth muscle. This effect may be due to its anti-muscarinic or antispasmodic activity [(18)]. Acetylcholine elicited contractions in ileum are believed to be mediated through M3receptors present on ileum. It was found that peppermint oil produced dose dependent inhibition of ileum contractions induced by acetylcholine. The parallel rightward shift in agonist concentration response curves of acetylcholine in presence of increasing concentrations of PO was indicating antispasmodic activity (anti-muscarinic). The inhibition may be due to the antagonism of cholinergic-muscarinic receptors or nonspecific spasmolytic action of PO. [(18)]

**CONCLUSION:**

While the bleeding amount did not significantly change, pain and its severity and all the clinical signs and symptoms decreased after taking peppermint extract. Because the side effect of herbal drugs is lower than other medicinal drugs, using mint is advised for treating dysmenorrhea symptoms. It can be concluded from the study that the PO possesses significant anti spasmodic activity that may be due to the M3-antagonis (cholinergic muscarinic-antagonism) on smooth muscles of chicken ileum. This may substantially benefit in the treatment of spasm and other intestinal muscular disorders.

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