Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20172737

Original Research Article

Evaluation and comparison of analgesic activity of essential oil of *Rosmarinus officinalis* and *Thymus vulgaris*: an experimental study

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Received: 26 April 2017
Accepted: 24 May 2017

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ABSTRACT

Background: Since the time of stone age herbs in its natural forms are used for a variety of medicinal purposes including the treatment of pain. Research in herbal medicine is in a relatively early phase. Herbal approaches usually have been pursued because of the perception that these therapies are gentler and cause fewer side effects than allopathic treatment. The aim was to evaluate and compare the analgesic activity of essential oil of Rosmarinus officinalis and *Thymus vulgaris* in wistar rats.

Methods: Wistar rats and hot plate method was used for this study. Control group (Group A) of 6 animals was given normal saline. Group B of 6 animals was given standard analgesic drug, aspirin (200mg/kg body weight). Group C of 6 rats was given REO at 100, 200, 300 and 400 mg/kg body weight on day 1, 2, 3 and 4 while Group D of 6 animals was given TEO at doses of 100, 200 and 300 mg/kg body wt. The analgesic activity of REO and TEO in terms of Response Time were noted and depicted in tabular form.

Results: Results were analyzed by one-way-Anova and Tukey tests. Analgesic effect of Rosemary oil found to be statistically significant at all four doses, 100, 200, 300 and 400mg/kg body wt compared to control group. TEO was found significantly analgesic at 100 and 200mg/kg body wt compared to control group but at 300mg/kg body it was found lethal. REO was found superior.

Conclusions: Analgesic effect of REO and TEO was not comparable to aspirin even at higher concentration like 400mg/kg (REO) but it was significantly more compare to control group.

Keywords: Aspirin, Analgesic activity, Hot plate analgesiometer, Rosemary essential oil, Thymus essential oil

INTRODUCTION

Research in herbal medicine is in a relatively early phase, and many studies have yielded only preliminary findings. Herbal approaches usually have been pursued because of the perception that many of these therapies are gentler and cause fewer side effects than pharmaceuticals. However, this perception must be tested in each case. It is important to know and remember that herbs contain active chemicals that may have side effects or interactions with foods and other drugs. For the management of pain, a constant research based on natural pharmacophores and its interaction with targets, has led to search of many potential therapeutic agents.[1]

Rosmarinus officinalis (Family Lamiaceae), popularly called rosemary, is a common household plant and grown in many parts of the world. It is an aromatic evergreen shrub and its leaves are similar to hemlock needles. The leaves are used as a flavoring agent in foods. It is native to the Mediterranean countries and Asia, but is reasonably hardy in cool climates. It can withstand droughts.[2]

Various parts of the rosemary plants are in use for the medicinal purpose since the stone age. Rosemary contains a number of phytochemicals, including rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, and the antioxidants carnosic acid and carnosol.[3]

These phytochemicals have antispasmodic, analgesic, antirheumatic, carminative, cholagogue, diuretic, expectorant, and antiepileptic effects.

Some of these chemical components also have anti-oxidant and antimicrobial property, and hence may protect against various forms of cancers and infections.[4] Its ethanolic preparation is highly lipid soluble and hence can be absorbed through the skin.

The genus Thymus, member of the Lamiaceae family, contains about 400 species of perennial aromatic, evergreen or semi-evergreen herbaceous plants with many subspecies, varieties, sub varieties and forms.[5]

Various studies have aimed to investigate the chemical composition and biological properties of the *T. vulgaris* essential oil (EO). According to European Pharmacopoeia 5.0 (Ph. Eur. 5.0).[6]

The minimum content of EO in *T. vulgaris* is 12mL/kg, but the chemical composition shows variations, six chemotypes being mainly reported, namely geraniol, linalool, gamma-terpineol, carvacrol, thymol and trans-thujan-4-ol/terpinen-4-ol.[7,8]

In addition to the flavoring properties determined by the constitutive active ingredients, the thymus EO exhibits significant antimicrobial activity as well as strong antioxidant properties.[7,9,10]

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[11]

In medical diagnosis, pain is regarded as a symptom of any unpleasant underlying condition.

Pain motivates the individual to withdraw from damaging situations, to protect a damaged body part while it heals, and to avoid similar experiences in the future.[12]

Commonly clinicians prescribe analgesics from category of non-steroidal-anti-inflammatory drugs. Apart from these allopathic treatments there are some herbal products, in which parts of a plant are used medicinally to treat many health problems including pain. Inclination towards herbal therapy is increasing in the community day by day.

Though research on herbal remedies is still in its early phases, many herbs are thought to reduce pain and inflammation. However, it should be used with caution.[13]

This study was planned to evaluate the analgesic effects of Rosemary essential oil (REO) and *Thymus vulgaris* essential oil (TEO) specially for the population not willing to take allopathic painkillers.

METHODS

Wistar rats were screened and selected by using hot plate method with a cut off time 30secs.

After selecting the animals, all 24 animals were acclimatized in the environment (25±3°C), with light/dark control each 12 hours (7 a.m. to 7 p.m.) and were placed in cages up to 6 rats and were provided with proper meal and water ad libitum. They were kept without any food 12 hours before the experiments, but water ad libitum.

The essential oil of Rosemary, essential oil of Thymus was purchased online from amazon.in and Tab. Aspirin and normal saline was bought from local medical store.

Then the animals were divided into 4 groups (n=6).

Groups A (Control) was given normal saline (NS) 0.5 ml orally. Group B was given standard drug aspirin at dose of 200mg/kg.[14]

Group C was given test drug, rosemary oil in increasing dose of 100mg/kg, 200mg/kg, 300mg/kg, 400mg/kg on 1st, 2nd, 3rd and 4th day.[15] Group D was given test drug, thymus essential oil in increasing dose of 100mg/kg, 200mg/kg and 300mg/kg on 1st, 2nd and 3rd day.

The dose of 300mg/kg body wt of TEO was found toxic to the animals hence we recorded the analgesic effect of TEO only upto dose 200mg/kg body wt and animals were not given dose 400mg/kg body wt unlike group C.

Eddy's hot plate analgesiometer apparatus was maintained at 55±0.50 degree centigrade. Animals were individually exposed and the reaction time they have spent to lick the footpad or any paw or jumping were recorded. The cut off time used were 30 seconds to avoid thermal injury. The observations were taken at 0, 30, 60, 90 and 120 minutes after drug treatments.

Response time for each drug and dose were depicted in tables and the analgesic activity of REO was compared with that of standard and control group and statistically analyzed by one way ANOVA. Multiple Comparison was done by Tukey Test. Software used in the analysis were SPSS 17.0 version and EPI-INFO 6.0 version.

RESULTS

The analgesic effect of REO and TEO is less compared to Aspirin but more compared to control. Both was found with significant analgesic effect. That means both are less potent herbal analgesics.

P value was found non significant at 0 min. But at 30mins and 60mins Group B was found significant as compared to Group A, C1, C2, C3, C4, D1, D2. At 90mins, Group B was found significant as compared to Group A, C1, C2,

C3, C4, D1, D2. C3 and C4 were significant as compared to C1, C2, D1 and D2 (Table 1). At 120mins Group B was found significant as compared to Group A, C1, C2, C3, C4, D1, D2.

C3 and C4 were significant as compared to C1, C2, D1, D2. D1 and D2 were found to be more significantly analgesic as compared to C1, C2 (Table 1).

Table 1: Mean and standard deviation (SD) of response time in groups.

Group		0 min	30min	60min	90min	120 min
A (NaCl) Control	Mean SD	4.16 0.98	4.16 0.98	4.16 0.98	4.16 0.98	4.16 0.98
B (Aspirin) Standard	Mean SD	4.16 0.98	7.83 1.32	9.66 1.50	11.16 1.60	13.33 1.50
C1 = REO 100mg/kg (Day 1)	Mean SD	3.5 1.22	3.5 1.22	4.5 1.22	4.66 1.03	4.66 1.03
C 2 =200mg/kg (Day 2)	Mean SD	3.5 1.22	3.5 1.22	4.5 1.22	4.66 1.03	4.5 1.04
C 3= 300mg/kg (Day 3)	Mean SD	3.33 1.21	4.83 1.16	5.66 0.81	7.16 1.94	7.33 1.86
C 4= 400mg/kg (Day 4)	Mean SD	3.66 1.5	4.33 1.03	5.83 1.16	7.33 0.81	9 0.89
D1 = TEO 100mg/kg (Day 1)	Mean SD	3.83 0.75	3.83 0.75	4.66 1.03	5.50 0.83	5.66 0.51
D2 =200mg/kg (Day 2)	Mean SD	3.83 0.75	5.16 0.40	5.33 0.51	6.16 0.40	6.50 0.54
P value		0.85, NS	0.0001, S	0.0001, S	0.0001, S	0.0001, S
Significant pairs			A vs B B vs C1, C2, C3, C4, D1, D2	A vs B B vs C1, C2, C3, C4, D1, D2	A vs B B vs C1, C2, C3, C4, D1, D2 C 1 vs C3, C4 C2 vs C3, C4	A vs B B vs C1, C2, C3, C4, D1, D2 C3 vs C2 C3 vs C1 C4 vs D1, D2

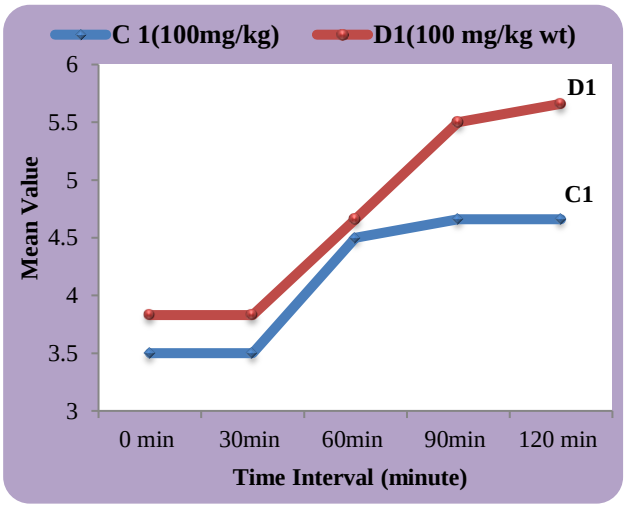

Figure 1: Result of Hot Plate Test for 100mg/kg dose of REO and TEO.

The results obtained show REO has analgesic activity which increases with increase in concentration upto 400mg/kg body wt. TEO has analgeisic activity which increases with increase in concentration upto 200mg/kg body wt and it was found lethal at the dose of 300mg/kg body wt (Figure 1 and 2).

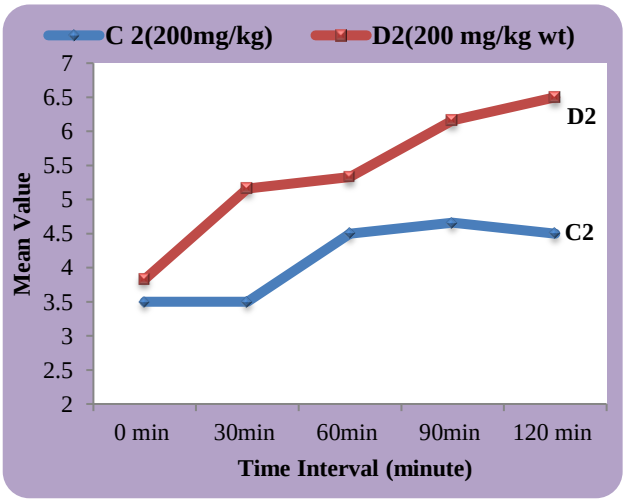

Figure 2: Result of Hot Plate Test for 200mg/kg dose of REO and TEO.

DISCUSSION

Essential oils are complex mixtures of volatile, liquid, lipophilic and odoriferous substances. The composition of an essential oil is genetically determinant, specific for a tissue or a characteristic of its development stage. In this study, we evaluated the efficacy of the essential oil obtained from *R. officinalis* and *Thymus vulgaris*.

For studying the analgesic effects, we performed the hot-plate analgesiometer which helps to measures animal nociceptive response latencies to thermal stimulus. Treating the animals with *Thymus vulgaris*, at a dose of 100mg/kg and 200mg/kg alters mouse latency to painful thermal stimulus in the hot-plate test. These findings suggest that peripheral mechanisms are involved in the antinociceptive activity of the extract.

The main chemical components of rosemary oil are a-pinene, borneol, b-pinene, camphor, bornyl acetate, camphene, 1,8-cineole and limonene. The major components of *Thymus vulgaris* p-cymene (8.41%), γ-terpinene (30.90%) and thymol (47.59%).

Thymus also contains carvacrol (ca.15%).

Thymus vulgaris has antispasmodic effect and does not have gastrointestinal complication, also it relieves gastrointestinal disorders such as ulcers, indigestion, constipation, flatulence, and asthma.[16] Our finding demonstrated that thymus vulgaris as well as ibuprofen significantly reduced primary dysmenorrhea compared with placebo.[17]

The results obtained in our study shows that Essential oil of *Rosemarinus officinalis* and *Thymus vulgaris* has analgesic activity which increases with increase in concentration upto 400mg/kg body wt and 200mg/kg body wt respectively though not comparable to Aspirin.

Chemical compounds found in the *T. vulgaris* essential oil possibly responsible for analgesic effect of Thymus is p-cymene, γ-terpinene and thymol [18,19]

Carvacrol has antinociceptive activity which can be associated to its antioxidant property. These effects are definitely related to the inhibition of prostaglandin synthesis by carvacrol, since this compound is a strong suppressor of cyclooxygenase (COX)-2 expression and a stimulator of the peroxisome proliferator activated receptors (PPAR) α and γ.

The result indicates the effectiveness and relative safety of REO and TEO for the treatment of conditions associated upto mentioned dose.

The group treated with REO has shown a significant inhibition both in the first and second phase compared to the control group (P <0.01). The effect was less than the group treated with Aspirin, confirming the peripheral effect of REO and suggesting an inhibition of prostaglandin synthesis.

The group treated with TEO has shown a significant inhibition both in the first and second phase compared to the control group (P <0.01). The effect was less than the group treated with REO as well as Aspirin, confirming mild peripheral effect of TEO and suggesting mild inhibition of prostaglandin synthesis.

Lucimara Romana Dipe de Faria carried out similar experiment and the result suggested that REO has an anti-inflammatory activity as well as peripheral analgesic activity, and has shown to be harmless to the gastric mucosa.

Hajar Salmalian et al, carried out a triple blind clinical study and demonstrated that *Thymus vulgaris* as well as ibuprofen significantly reduced primary dysmenorrhea compared with placebo.

Gonzalez-Trujano et al, carried out rat studies using several experimental models of pain. Intraperitoneal injection of rosemary extract significantly reduced writhing of rats compared to controls, suggesting reduction of spasmodic pain.[20]

Omidvar et al, studied the effect of fennel on pain intensity in dysmenorrhoea and found 52 percent of patients in the study group (vs. 8% placebo) considered the effect of treatment excellent.[17] Iravani's study revealed that the effect of *Thymus vulgaris* 2% in the reduction of the severity of dysmenorrhea was more than *Thymus vulgaris* 1%.[21]

CONCLUSION

Analgesic effect of *REO* and TEO was not comparable to aspirin even at higher concentration like 400mg/kg (REO) but it was significantly more compare to control group. That means these are weak analgesics. TEO was found more potent analgesic than REO but at the same time TEO was fond lethal to rats at dose of 300 mg/kg body weight.

Recommendations

Study of Analgesic effect of Rosemary essential oil is required in the clinical set up so that we may have an herbal analgesic preparation for the patient suffering from mild pain and having choice for the herbal medication.

ACKNOWLEDGMENTS

Authors would like to thanks to the HOD Dr. S.S Pathak, Dr. Vijay Babar, Kumar Popatkar, keeper animal house, a student Dr. Mahesh Jain and entire department of pharmacology for their untiring support. Also authors would like to extend their gratitude towards the institution for all the opportunities provided for research.

Funding: Funded by DMIMS (DU), Sawangi (Meghe), Wardha, Maharashtra
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Animal Ethical Committee

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Cite this article as: Jha AR, Paul S. Evaluation and comparison of analgesic activity of essential oil of *Rosmarinus officinalis* and *Thymus vulgaris*: an experimental study. Int J Basic Clin Pharmacol 2017;6:1718-22.