ผลของการดมน้ำมันระเหยเทพทาโรที่มีต่อระบบประสาทอัตโนมัติและสภาวะอารมณ์ของมนุษย์

The Effects of Cinnamomum porrectum Essential Oil Inhalation on Human Autonomic Nervous System and Emotional States

นิดา นุ้ยเด็น[1] วินัย สยอวรรณ[2] วรสิทธิ์ ศิริพรพาณิชย์[3] ธีเวลดี เกรบิจิโอกริส โฟโต[4] ชนิดา พลานุเวช[1] นิจศิริ เรืองรังษี*[1]

Nida Nuiden[1], Winai Sayorwan[2], Vorasith Siripornpanich[3], Tewelde G. Foto[4], Chanida Palanuvej[1], Nijsiri Ruangrungsi*[1]

[1]วิทยาลัยวิทยาศาสตร์สาธารณสุข จุฬาลงการณ์มหาวิทยาลัย กรุงเทพมหานคร ประเทศไทย 10330

[1]College of Public Health Sciences, Chulalongkorn University, Bangkok, Thailand, 10330

[2]วิทยาลัยเทคโนโลยีทางการแพทย์และสาธารณสุข กาญจนาภิเษก นนทบุรี ประเทศไทย 11150

[2]Kanchanabhisek Institute of Medical and Public Health Technology, Nontaburi, Thailand, 11150

[3]สถาบันชีววิทยาศาสตร์โมเลกุล มหาวิทยาลัยมหิดล นครปฐม ประเทศไทย 73170

[3]Research Center for Neuroscience, Institute of Molecular Biosciences, Mahidol University, Nakhonpathom, Thailand, 73170

[4]คณะสาธารณสุขศาสตร์ วิทยาลัยนานาชาติเซนต์เทราซา นครนายก ประเทศไทย 26120

[4]Faculty of Public Health, St Theresa International College, Nakhonnayok, Thailand, 26120

บทคัดย่อ

Cinnamomum porrectum หรือที่รู้จักกันทั่วไปในชื่อเทพทาโร หรือ Safrole laurel พบได้ในประเทศแถบเอเชียและถูกใช้ในการแพทย์แผนไทย การวิจัยครั้งนี้มีวัตถุประสงค์เพื่อศึกษาผลของการดมน้ำมันระเหยเทพทาโร ที่มีต่อระบบประสาทอัตโนมัติและสภาวะทางอารมณ์ การวิจัยครั้งนี้เป็นการศึกษาวิจัยเชิงทดลองแบบ A-B โดยมีกลุ่มตัวอย่างที่มีสุขภาพดี 25 คน อายุระหว่าง 20 ถึง 35 ปีได้รับการคัดเลือกเข้ากลุ่ม กลุ่มตัวอย่างกรอกแบบสอบถามเกี่ยวกับสภาวะทางอารมณ์ก่อนและหลังการดมน้ำมันระเหยเทพทาโรที่เข้มข้นร้อยละ 8 ผ่านหน้ากากพลาสติก (2 มล. / นาที) ประเมินผ่านระบบประสาทอัตโนมัติ บันทึกด้วยเครื่องวัดสัญญาณชีพรุ่น BIOM7000 วิเคราะห์ข้อมูลโดยใช้สถิติเชิงพรรณนา paired t-test ผลจากระบบประสาทอัตโนมัติ บอกได้ว่า ค่าความดันโลหิต systolic และ diastolic หลังจากการดมน้ำมันระเหยเทพทาโรเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ (p-value <0.001) จาก 104.55 (±7.54) เป็น 106.01 (± 7.46) มิลลิเมตรปรอท และจาก 63.55 (±5.10) เป็น 65.24 (± 5.11) มิลลิเมตรปรอท หลังจากการดมน้ำมันระเหยเทพทาโรอัตราการเต้นของหัวใจเฉลี่ยเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ (p-value <0.001) จาก 78.25 (±9.1) เป็น 79.83 (± 9.1) ครั้งต่อนาทีและอัตราการหายใจเฉลี่ยเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ (p-value <0.008) จาก 17.02 (±1.98) เป็น 18.06 (± 2.16) ครั้งต่อนาที สภาวะทางอารมณ์คะแนนเฉลี่ยของความรู้สึกกระปรี้กระเปร่าและความรู้สึกสดชื่นเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติที่ (p-value <0.001) จาก 3.48 (±2.48) เป็น 5.97 (± 1.87) และ จาก 4.15 (±2.53) เป็น 6.63 (± 2.06) ตามลำดับ หลังจากการสูดดมน้ำมันระเหยเทพทาโร สรุปได้ว่า น้ำมันระเหยเทพทาโรสามารถกระตุ้นให้เกิดผลต่อระบบประสาทอัตโนมัติและสภาวะทางอารมณ์ได้

คำสำคัญ: น้ำมันระเหยเทพทาโร ระบบประสาทอัตโนมัติ สภาวะทางอารมณ์ การกระตุ้น

Corresponding Author: E-mail: nijsiri.r@chula.ac.th

วันที่รับ (received) 5 ม.ค. 62 วันที่แก้ไขเสร็จ (revised) 20 พ.ค. 62 วันที่ตอบรับ (accepted) 25 พ.ค. 62

Abstract

Cinnamomum porrectum (Roxb.) Kosterm commonly known as Thep-Ta-Ro and Safrole laurel is found in Asian countries and used in traditional Thai medicine. The aim of this research is to investigate the effects of C. porrectum essential oil inhalation on autonomic nervous system (ANS) and emotional states. This research is an experimental study using A-B design. Twenty-five healthy participants aged between 20 and 35 years old were recruited. The participants filled out a questionnaire on emotional states before and after they inhaled 8% of C. porrectum essential oil via face mask (2 ml/min). ANS parameters were recorded using BIOM7000 Patient Monitor. Data were analyzed using paired simple t-test. Mean changes of the ANS parameters and emotional states of participants were compared before and after the inhalation of C. porrectum oil. The mean systolic and diastolic blood pressure increased significantly from 104.55 (±7.54) to 106.01 (±7.46) mmHg (p-value <0.001) and from 63.55 (±5.10) to 65.24 (±5.11) mmHg (p-value <0.001) respectively. Similarly, the mean heart rate increased significantly from 78.25 (±9.1) to 79.83 (±9.1) mmHg (p-value <0.001) and the mean respiratory rate increased significantly from 17.02 (±1.98) to 18.06 (±2.16) bpm (p-value <0.008). Regarding the emotional states, the mean scores of active feelings increased significantly from 3.48 (±2.48) to 5.97 (±1.87) (p-value <0.001) and the mean scores of fresh feelings increased significantly from 4.15 (±2.53) to 6.63 (±2.06) (p-value <0.001). It can be concluded that C. porrectum essential oil seems to have stimulating effects on ANS parameters and emotional states.

Keywords: Cinnamomum porrectum (Roxb.) Kosterm, Safrole laurel, autonomic nervous system, emotional states, stimulating effect

Introduction

According to the European Pharmacopoeia, an essential oil means a manufactured product from pure, identified raw materials of plant origin obtained from hydro-distillation and steam distillation or mechanical processes. Essential oils are characterized by hundreds of compounds with different structures and functional groups. Essential oils have become more popular around the world since they are in high demand for their use in the industries of flavors, fragrances, cosmetics, healthcare and aromatherapy[1]. Aromatherapy provides the knowledge on how complex mechanisms of the essential oils work to cure some symptoms of diseases. It refers to the use of essential oils which can be extracted from plants with therapeutic properties[2,3]. It is the therapeutic use of herbs and flowers in the form of essential oils to treat, to balance, to relax, to stimulate and to rejuvenate human mind and body[4]. Aromatherapy is divided into 3 types: aesthetic, clinical and holistic. Aesthetic aromatherapy is defined as the use of an essential oil for merely the pleasure of its aroma while clinical aromatherapy is a treatment focusing on specific health issue and usually measuring the impact of the treatment. In contrast, holistic aromatherapy is the use of mixed essential oils to promote, to relax and to energize human mind, body and spirit[5]. Aromatherapy has been used and integrated as a part of traditional Thai medicine including foot reflexology[6]. It has been applied to treat patients and maintain holistic health.

Cinnamomum porrectum (Roxb.) Kosterm. is found in Asian countries such as India, Myanmar, China and Thailand. Its common name is Thep-Ta-Ro, Safrol laurel and Citronella laurel. It is a scarce medicinal and aromatic tree growing in southern

Thailand including Krabi, Phang Nga, Pattalung and Trang provinces. It is a medium-sized to large, deciduous tree up to 4.5 meters tall. Its seed is considered as one of the most popular aromatherapy and spa oils. C. porrectum has been used in traditional Thai medicine to relieve indigestion and upset stomach, to alleviate fever and to reduce intestinal and gastric gas[7,8]. Its essential oil has been used as a flavoring agent in food and beverage industry and an ingredient of perfumes and soaps. It can be used in soft drinks with the limit based on food additive regulations[9]. Previous studies found that the C. porrectum essential oil consisted of safrole, elemicin and methyl eugenol[10]. The therapeutic properties of the C. porrectum essential oil are antioxidant, antibacterial and antimicrobial and anti-inflammatory[11-14]. Because of its therapeutic properties, the C. porrectum essential oil has been developed in various forms such as emulgel topical dosage forms for pharmaceutical purposes[15].

Research gap

A number of research studies have been conducted on the effects of essential oils on emotional states and physiological activities. However, the research studies on the effects of C. porrectum on autonomic nervous system (ANS) and emotions are still limited. Therefore, the researchers aim to conduct an A-B design to investigate the effects of the C. porrectum essential oil inhalation on ANS and emotional states.

Methodology

Sample size

To estimate the sample size for this study, the sample size calculation formula for one sample problems was taken according to Lemeshow 1990, and a previous related study, Sayorwan 2011, which was referred for completing the unknown parameters[16,17.] The mean and SD values of emotional state changes during, resting, sweet almond oil and rosemary oil inhalations were used to obtain pooled variance. Significance level of lower than 0.05 (Z_a = 1.96) and a power of test at 80% were used. After adjusting for a 10% drop-out, the total population number was 25 participants as an appropriate sample size.

Research design

This research was an experimental study which was carried out using an A-B design. This research is part of a bigger project that examined the effect of inhalation of 4 different essential oils on ANS and emotional states. For the 4 experiments, 100 healthy participants were recruited from the general public and 25 of them were assigned for this study randomly. Healthy participants volunteered to participate in this study. 25 participants aged between 20 and 35 years old were recruited from the general public. The research was conducted at Kanchanabhisek Institute of Medical and Public Health Technology.

Ethical considerations

The research was approved by the Ethics Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University on 8 February, 2018 with ethics number COA No. 034/2561. The researchers obtained written informed consent before enrolling the participants into the intervention. The researchers explained all the aspects of the study and the participants were asked to read and sign the consent. They were informed that they had the rights to withdraw from the study anytime they wished to.

Inclusion and exclusion criteria

A total of 25 healthy participants aged between 20 and 35 years with normal cardiovascular health were recruited. They had a normal range of body mass index (BMI) between 18.5 and 22.9 kg/m^2

based on WHO and Asian criteria values[18]. Only right-handed participants were recruited and evaluated by the Edinburgh Handedness Inventory scale[19]. A normal sense of smell of all the participants was screened using the n-butyl alcohol test[20]. The personal health status of all the participants which included weight, height and blood pressure was also recorded. All the participants were nonsmokers, without any symptoms of upper respiratory infection, hypertension or cardiovascular disease. They should not have current or past history related to neurological illness, epilepsy and loss of consciousness longer than 30 minutes. They should take neither central nervous system (CNS) medication nor sedative drugs. Each participant was asked to inhale the mixture of sweet almond oil and the C. porrectum oil to fill out the pleasantness from "Odor familiarity five-point Likert scale". Only the potential participants who indicated the oil pleasantness within the range of 2-4 were recruited as the research participants. The participants who were allergic to essential oils or had a headache were excluded from the experiment.

Essential oil

The natural C. porrectum oil used in this study was obtained from Wood Craft Products Group's Tham Le KhaoKob, Trang province, Southern Thailand. The sweet almond oil was obtained from Thai China Flavours and Fragrances Industry. The chemical compounds of C. porrectum oil extracted from its root were analyzed by gas chromatography/mass spectrometry (GC/MS) equipped with Finnigan DSQ MS detector (USA), Thermo Finnigan model Trace GC Ultra. The researchers matched its mass spectra and retention times indicated in NIST05 library to identify its chemical compounds. Then, the researchers computed their percentage from GC peak area[21,22]. The equipment is located in the laboratory in the College of Public Health Sciences, Chulalongkorn University. The results indicated that the C. porrectum oil consisted of 98.33% of safrole, 1.5% of elemicin and 0.17% of methyl eugenol.

Essential oil delivery

Sweet almond oil was used as base oil to dilute the C. porrectum oil. Sweet almond oil is often used as base oil in clinical research and aromatherapy: and its odorless property makes it suitable for research and aromatherapy base oil[23]. The C. porrectum oil (8% in the sweet almond oil) was delivered from oxygen pump system through a plastic tube via face mask (2ml/min).

Outcome instruments

Four ANS parameters including skin temperature, respiratory rate, heart rate and blood pressure were recorded by BIOLIGHT M7000 Multi-Parameter Patient Monitor – BIOM7000 in real time. Based on what was used in previous study, Sayorwan, 2011 a modified Geneva Emotion and Odor Scale (GEOS) was used[16]. The questionnaire procedure was proposed to evaluate the aspects of the emotions of each participant. To express their subjective emotional feelings, the participants were asked to point out the magnitude of the feelings on the GEOS. These feelings were categorized in to 5 factors: pleasant, unpleasant, sociosexual, relaxation and refreshing feelings in which they, in turn, were expanded into 12 items.

Procedures

The researchers asked each participant to sit comfortably in semi-reclining chair with quiet, air-conditioned (24 ± 1 °C), 50-65% humidity in a pre-ventilated room. The experiment was conducted between 8.00 a.m. and 12.00 a.m. to minimize circadian variation. Each participant was tested separately to avoid the mutual distraction. The room was re-ventilated with fresh air for 15 minutes before the next experiment. First, the participants were asked to complete a questionnaire on emotional states before the inhalation. Second, they were attached to the equipment to record the vital signs. Third, they

inhaled sweet almond oil for 10 minutes and ANS parameters were recorded. Fourth, they were asked to fill out the questionnaire on emotional states again. Fifth, the participants inhaled a mixture of the C. porrectum oil and sweet almond oil for 10 minutes and ANS parameters were recorded. Sixth, they were asked to fill out the questionnaire on emotional states for the third time and the experiment was completed.

Data analysis

The researchers analyzed the data on the effects of the C. porrectum oil on ANS parameters and emotional states in the following steps: before the treatment, after sweet almond oil inhalation and after C. porrectum oil inhalation. The data were analyzed with STATA version 14 statistical software by using paired simple t-test. A p-value < 0.05 was considered significant. The researchers conducted a paired t-test on the data related to blood pressure, heart rate, skin temperature, respiratory rate and the rating of emotional states. The results before the treatment were compared with the results after almond oil inhalation which were again compared with the results after C. porrectum inhalation.

Results

Demographic data

The mean (SD) of the participants' age, height, weight, and BMI were 20.72 (1.84) years old, 1.60 (0.06) m, 51.96 (5.22) Kg, 20.36 (1.44) Kg/m^2 respectively.

ANS parameters

Table 1 showed the mean (SD) values of the ANS parameters in the experiment. It illustrated the mean values of ANS parameters during the three phases of the experiment: resting, the inhalation of sweet almond oil and C. porrectum oil (8% in sweet almond oil). The ANS parameters after the participants inhaled sweet almond oil were compared to the results obtained after the participants inhaled C. porrectum oil and found that the mean systolic and diastolic blood pressures increased significantly from 104.55(±7.54) to 106(±7.46) mmHg and from 63.55(±5.10) to 65.42(±5.11) mmHg respectively, both with a p-value of <0.001. The mean heart rate was 78.25 (±9.1) bmp after sweet almond oil inhalation and after C. porrectum oil inhalation, it increased significantly to 79.83 (±9.1) bmp (p-value <0.001). After the C. porrectum oil inhalation, the mean respiratory rate increased significantly from 17.02 (±1.98) bmp to 18.01 (±2.16) bmp (p-value <0.008).

Emotional state response

The effects on emotional state response were shown in Table 2 which displayed the mean values of emotional states during resting, the inhalation of sweet almond oil and the C. porrectum oil (8% in sweet almond oil). Regarding the emotional states, the mean scores of active feelings after the sweet almond oil inhalation were 3.48 (±2.48) and increased significantly to 5.97 (±1.87) after the C. porrectum oil inhalation (p-value <0.001). The mean scores of fresh feelings after the sweet almond oil inhalation were 4.15 (±2.53) and increased significantly to 6.63 (±2.06) after the C. porrectum oil inhalation (p-value <0.001).

Discussion

In this study, C. porrectum essential oil was administered by inhalation to healthy participants. The researchers recorded blood pressure, heart rate, skin temperature and respiratory rate as the indicators of the ANS system. Moreover, the participants were asked to subjectively rate their emotional states in terms of good, bad, active, drowsy, fresh, relaxed, stressed, frustrated, romantic, annoyed, calm and disgusted feelings in order to measure subjective behavioral arousal.

Clinical research studies are conducted on the effects of the essential oil inhalation on humans

Table 1. Parameters of autonomic nervous system during resting, the inhalation of sweet almond oil and C. porrectum essential oil

Parameters	n	Rest		Sweet almond oil (SO)		C. porrectum (CIN)		p-value rest and SO	p-value SO and CIN
		Mean	SD	Mean	SD	Mean	SD		
Systolic blood pressure (mmHg)	25	104.80	7.14	104.55	7.54	106.01	7.46	0.605	0.001*
Diastolic blood pressure (mmHg)	25	64.03	5.42	63.55	5.10	65.42	5.11	0.401	0.001*
Heart rate (bpm)	25	79.24	9.55	78.25	9.10	79.83	9.10	0.036*	0.001*
Skin temperature (°C)	25	31.78	1.10	31.76	1.17	31.68	1.07	0.538	0.646
Respiratory rate (bpm)	25	17.16	1.72	17.02	1.98	18.06	2.16	0.317	0.008*

* Significant difference, p-value < 0.05, SO = sweet almond oil, CIN = C. porrectum,
mmHg = millimeters of mercury, bpm = breaths per minute

Table 2. Parameters of emotional states during resting, the inhalation of sweet almond oil and C. porrectum essential oil

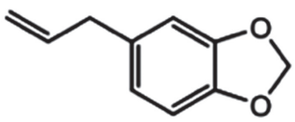
Parameters	n	Rest		Sweet almond oil (SO)		C. porrectum (CIN)		p-value rest and SO	p-value and CIN
		Mean	SD	Mean	SD	Mean	SD		
1. good	25	6.69	2.17	5.79	2.43	4.88	2.95	0.044*	0.159
2. bad	25	2.14	2.40	1.94	1.95	2.80	2.85	0.661	0.161
3. active	25	3.78	2.04	3.48	2.48	5.97	1.87	0.529	0.001*
4. drowsy	25	2.90	2.51	2.98	2.24	2.87	2.10	0.865	0.761
5. fresh	25	4.90	2.28	4.15	2.53	6.63	2.06	0.203	0.001*
6. relaxed	25	5.73	2.13	4.75	2.54	4.67	2.75	0.151	0.911
7. stressed	25	2.17	2.17	2.45	2.35	2.34	2.24	0.474	0.852
8. frustrated	25	2.35	2.29	2.46	2.25	2.78	2.54	0.808	0.621
9. romantic	25	2.24	1.93	3.20	2.48	2.85	2.42	0.020*	0.413
10. annoyed	25	1.54	1.77	1.91	2.08	2.04	2.3036	0.298	0.805
11. calm	25	4.83	2.51	5.21	2.41	4.70	2.7863	0.336	0.404
12. disgusted	25	0.87	1.32	1.25	1.86	1.52	2.1139	0.297	0.616

*Significant difference, p-value < 0.05, SO = sweet almond oil, CIN = C. porrectum

which are divided into physiological and psychological effects. The physiological effects can be measured by the ANS parameters while the psychological effects can be assessed by the questionnaires on emotional states. The essential oil inhalation, which affects the cortical functions and activities directly through the olfactory system, causes the cortical arousal leading to positive or negative emotional states and the autonomic arousal including blood pressure, heart rate, respiratory rate, and skin temperature[24].

The results of this research revealed that the C. porrectum essential oil inhalation affected the ANS parameters as it increased the level of ANS arousal. Significant increases in mean systolic and diastolic blood pressures, heart rate and respiratory rate were observed. The research results were consistent with previous studies. Stern et al., 2001 reported that the increases in the autonomic arousal by essential oil inhalation could be interpreted as stimulating effects of the essential oils[25].

The GC/MS analysis of C. porrectum root in this study showed the main chemical compound as safrole with 98.33%. A possible cause of the feeling of stimulating effects after the inhalation of C. porrectum essential oil, therefore, might be the existence of safrole in the essential oil. Safrole (1-allyl-2, 5-dimethoxy-3, 4-methylenedioxybenzene) is one of the alkenylbenzene derivatives.



safrole

(Figure 1) The structural formulas of The alkenylbenzene safrole

The alkenylbenzene compounds, which could be found naturally in various essential oils from plants, were found to have effects on nervous stimulating activity and could be used as a precursor in the illicit MDMA (3, 4-methylenedioxy-N-methylamphetamine) synthesis[26]. Moreover, safrole can be widely applied in the chemical industry as a synthetic precursor of piperonyl butoxide, piperonal and drugs including tadalafil, cinoxacin and levodopa. The versatile nature of its structure makes it an important chemical precursor in the production of multiple drugs with various pharmacological activities[27]. An animal study on the effect of safrole, conducted in rats and guinea pigs, showed it has a stimulating effect. After the administration of safrole, subjects remained active and excited up to two hours[28].

The mean values of the emotional states during resting, the inhalation of sweet almond oil and C. porrectum essential oil (mixed with sweet almond oil) are shown in Table 2. After the C. porrectum essential oil inhalation, the participants felt more active and fresher based on their self-evaluated questionnaires on their emotional states. These results revealed that safrole, which is a major compound in the C. porrectum essential oil, could have been played a main role in inducing pleasant and refreshing emotional states among the participants. Previous evidence showed that the substances from herbal plants and spices such as nutmegs and cloves containing the alkenylbenzene derivatives induced psychoactive metabolites which were similar to stimulants such as amphetamines. Furthermore, Tajuddin et al., investigated the stimulating effects

of nutmegs and cloves in mice. The researchers found that both nutmegs and cloves could enhance mounting behavior and mating performance in male significantly[29]. This effect is also observed in lower form of animals. The exposure of male Mediterranean fruit flies to ginger oil increases the mating success of the insects[30]. Another research also states that high doses of sassafras oil with Safrole as a major chemical compound is strong stimulating, sexually exciting and even consciousness altering[31].

Conclusions

In conclusion, this research contributes to an existing body of knowledge on the effects of the essential oil inhalation. In particular, C. porrectum essential oil could have stimulating effects on ANS parameters and emotional states by increasing systolic and diastolic blood pressures, heart rate and respiratory rate as well as increasing active and fresh feelings.

Recommendations for Further Study

1. Further studies should be conducted to confirm its stimulating effects as that C. porrectum essential oil with safrole as a major compound could be reintroduced to be used as modern medicines including psychotherapy.

Applications for this study

1. C. porrectum essential oil could be applied as a treatment for those who suffer from depression based on a higher number of patients with depression nowadays[32].

2. C. porrectum essential oil may be applied as an herbal inhalant to feel fresh among the general public so that it can help promote the widespread use of Thai herbal medicine.

Acknowledgements

The researchers would like to express gratitude to Graduate School, Chulalongkorn University for the scholarship from the 90th Anniversary of Chulalongkorn University (Ratchadaphiseksomphot Endowent Fund); Thai Traditional Knowledge Fund, Department of Thai Traditional and Alternative Medicine, Ministry of Public Health for their research grants; Thaksin University for the scholarship from Human Resources Development Fund; Kanchanabhishek Institute of Medical and Public Health Technology for assistance and technical support and College of Public Health Science, Chulalongkorn University for the research equipment.

References

1. Do TK, Hadji-Minaglou F, Antoniotti S, Fernandez X. Authenticity of essential oils. TrAC Trends in Analytical Chemistry. 2015 Mar 1;66: 146-57.
2. Schnaubelt K. Medical aromatherapy: Healing with essential oils. North Atlantic Books; 2013 Jul 23.
3. Price L, Price S. Aromatherapy for Health Professionals E-Book. Elsevier Health Sciences; 2011 Nov 11.
4. Phungsoonthorn W, aromatherapy: how plants and oils help you. Proceedings of The 2015 International Symposium on Wellness and Aromatherapy Conference; 2015 July 23-24, Thailand. Rangsit University 2015.
5. Buckle J. Clinical aromatherapy: essential oils in healthcare. Elsevier Health Sciences; 2014 Nov 14.
6. Apichet K, Ounprasertpong L, Noppawan Piasea N. Secondary Data Analysis: Effects of Behavioral Modification Program and Foot Reflexology Integrated with Medication Use on Blood Pressure Level in Persons with Hypertension. Journal of The Royal Thai Army Nurses. 2017; 18(1): 58-65. (in Thai).

7. Uthairatsamee S, Soonthornchareonnon N, Wiwat C, Pipatwattanakul D. Antioxidant and antibacterial activities of the extracts from different parts of Cinnamomum porrectum (Roxb.) Kosterm. InProceedings of the 49th Kasetsart University Annual Conference, Kasetsart University, Thailand, 1-4 February, 2011. Volume 8. Subject: Natural Resources and Environment 2011 (pp. 107-115). Kasetsart University.
8. The Forest Herbarium, Royal Forest Department. Thai Plant Names Tem Smitinand. Revised ed. Bangkok: Prachachon Co., 2001
9. Choong YM, Lin HJ. A rapid and simple gas chromatographic method for direct determination of safrole in soft drinks. Journal of Food and Drug Analysis. 2001;9(1)
10. Sukcharoen O, Sirirote P, Thanaboripat D. Control of aflatoxigenic strains by Cinnamomum porrectum essential oil. Journal of food science and technology. 2017 Aug 1;54(9): 2929-35
11. Phongpaichit S, Kummee S, Nilrat L, Itarat A. Antimicrobial activity of oil from the root of Cinnamomum porrectum. Songklanakarin J Sci Technol. 2006;29:11-6.
12. Uthairatsamee S, Soonthornchareonnon N, Wiwat C, Pipatwattanakul D. Antioxidant and antibacterial activities of the extracts from different parts of Cinnamomum porrectum (Roxb.) Kosterm. InProceedings of the 49th Kasetsart University Annual Conference, Kasetsart University, Thailand, 1-4 February, 2011. Volume 8. Subject: Natural Resources and Environment 2011 (pp. 107-115). Kasetsart University.
13. Buru AS, Pichika MR, Neela V, Mohandas K. In vitro antibacterial effects of Cinnamomum extracts on common bacteria found in wound infections with emphasis on methicillin-resistant Staphylococcus aureus. Journal of ethnopharmacology. 2014 May 14;153(3): 587-95.
14. Palanuvej C, Werwatganone P, Lipipun V, Ruangrungsi N. Chemical composition and antimicrobial activity against Candida albicans of essential oil from leaves of Cinnamomum porrectum. JOURNAL OF HEALTH RESEARCH. 2006 Mar 1;20(1):69-76
15. Werawatganone, P, Palanuvej C, Lipipun V, Ruangrungsi N, Thep-ta-ro essential oil in solution and emulgel dosage forms. JOURNAL OF HEALTH RESEARCH. 2006 Mar 1;20(1):77-86.
16. Sayorwan W, Effects of Selected Volatile Oils Commonly Used in Thailand on Physiological Activities and Emotions [dissertation]. Chulalongkorn University;2011.
17. Lemeshow S, Hosmer DW, Klar J, Lwanga SK. Organization WH. Adequacy of sample size in health studies. Chichester: Jhon & wiley Son. 1990.
18. Llido LO, Mirasol R. Comparison of body mass index based nutritional status using WHO criteria versus “Asian” criteria: report from the Philippines. PhilSPEN Online JParenter Enteral Nutr. 2011:1-8.
19. Hummel T, Mohammadian P, Kobal G. Handedness is a determining factor in lateralized olfactory discrimination. Chemical senses. 1998 Oct 1;23(5):541-4.
20. Cain WS. Testing olfaction in a clinical setting. Ear, nose, & throat journal. 1989 Apr;68(4): 316-22.

21. McMaster MC. LC/MS: a practical user's guide. John Wiley & Sons; 2005 Aug 8.
22. Hicks RP. Handbook of GC/MS Fundamentals and Applications By Hans-Joachim Hübschmann. Wiley-VCH, Weinheim, Germany. 2001. xvi+ 591 pp. 17.5× 24.5 cm. ISBN 3-529-30170-4. $150.00.
23. Venturi M, Venturi-Jackson T, inventors. Therapeutic blended oil composition and method. United States patent application US 11/346,033. 2007 Aug 2.
24. Hongratanaworakit T. Physiological effects in aromatherapy. Songklanakarin J Sci Technol. 2004;26(1):117-25.
25. Stern RM, Stern RM, Ray WJ, Quigley KS. Psychophysiological recording. Oxford University Press, USA; 2001.
26. Alajlouni AM, Al_Malahmeh AJ, Kiwamoto R, Wesseling S, Soffers AE, Al-Subeihi AA, Vervoort J, Rietjens IM. Mode of action based risk assessment of the botanical food-borne alkenylbenzene apiol from parsley using physiologically based kinetic (PBK) modelling and read-across from safrole. Food and Chemical Toxicology. 2016 Mar 1;89: 138-50.
27. Lima LM. Safrole and the versatility of a natural biophore. Rev Virtual Quim. 2015 Mar 1;7(2): 495-538.
28. Oswald ES, Fishbein L, Corbett BJ, Walker MP. Urinary excretion of tertiary amino methoxy methylenedioxy propiophenones as metabolites of myristicin in the rat and guinea pig. Biochimica et Biophysica Acta (BBA)-General Subjects. 1971 Aug 19;244(2):322-8.
29. Ahmad S, Latif A, Qasmi IA. Aphrodisiac activity of 50% ethanolic extracts of Myristica fragrans Houtt.(nutmeg) and Syzygium aromaticum (L) Merr. & Perry.(clove) in male mice: a comparative study. BMC Complementary and Alternative Medicine. 2003 Dec;3(1):6.
30. Shelly TE, McInnis DO, Pahio E, Edu J. Aromatherapy in the Mediterranean fruit fly (Diptera: Tephritidae): sterile males exposed to ginger root oil in prerelease storage boxes display increased mating competitiveness in field-cage trials. Journal of Economic Entomology. 2004 Jun 1;97(3):846-53.
31. Rätsch C, Müller-Ebeling C. The encyclopedia of aphrodisiacs: Psychoactive substances for use in sexual practices. Simon and Schuster; 2013 Feb 3.
32. Boonkerd S, Rabampho P, Deenuanpanao S, Naksranoi S, Paikoh K. The Relationship between Social Support and Depression of the Elderly in the Elderly Home. Journal of the Royal Thai Army Nurses. 2018; 19(1): 182-189. (in Thai).