Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 13, (2024)
https://www.jneonatalsurg.com

OPEN ACCESS

Promoting Peaceful Sleep: Exploring the Therapeutic Potential of Microemulsion with Cedarwood and Passion Flower Essential Oils for Insomnia Relief

Goswami Raksha[1], Jain Neetesh Kumar[1]

[1]Department of Pharmacology, Faculty of Pharmacy, Oriental University Indore

Correspondence author:

Raksha Goswami

Email ID : rakshag23@gmail.com

Cite this paper as: Goswami Raksha, Jain Neetesh Kumar, (2024) Promoting Peaceful Sleep: Exploring the Therapeutic Potential of Microemulsion with Cedarwood and Passion Flower Essential Oils for Insomnia Relief *Journal of Neonatal Surgery*, 13, 427-431.

ABSTRACT

Aim: This research explores the pharmacological efficacy of polyherbal microemulsions specifically designed to alleviate insomnia.

Method: Carefully selected herbs with sedative, anxiolytic, and sleep-enhancing properties were blended to formulate polyherbal microemulsions. An essential step in formulation involved optimizing the proportions of oil, water, surfactant, and co-surfactant to ensure stability and enhance active ingredient delivery. The system's suitability for systemic use was validated through physicochemical analysis, including droplet size and zeta potential assessment. In vivo evaluations using insomnia-induced animal models revealed improvements in sleep-related parameters such as sleep latency, duration, and quality.

Result: The results contribute to growing evidence supporting the therapeutic potential of polyherbal microemulsions for insomnia treatment. By harnessing the synergistic properties of herbal constituents in an optimized delivery system, these formulations offer a holistic method to reestablish sleep patterns while minimizing adverse effects. Further clinical trials are necessary to validate these findings and encourage the integration of such formulations into mainstream insomnia therapies.

Keywords: *Insomnia, Behavioral assays, Anxiety, Herbal therapies, Polyherbal microemulsions*

1. INTRODUCTION

Insomnia, a prevalent sleep disorder, is marked by difficulty falling asleep, staying asleep, or achieving restorative sleep despite adequate opportunities, often resulting in substantial daytime dysfunction. The underlying mechanisms of insomnia involve complex neurobiological, psychological, and environmental interactions. (1)

Neurobiological Aspects: A central feature of insomnia is hyperarousal, characterized by elevated cognitive and neural activity. Those affected frequently show increased metabolic rate, heart rate, and cortisol levels. Neuroimaging has demonstrated heightened activity in brain regions associated with arousal, further substantiating this connection (2,3).

Circadian Disruptions: Misalignment of circadian rhythms significantly contributes to sleep disturbances. Factors like irregular schedules, artificial light exposure, and lifestyle choices can disrupt these rhythms, worsening insomnia (4).

Neurotransmitter Alterations: Changes in neurotransmitters, particularly gamma-aminobutyric acid (GABA), are crucial in sleep regulation. GABA deficiency reduces inhibitory control, thereby promoting insomnia symptoms (5).

Psychological Influences: Stress and anxiety activate the physiological stress response, heightening arousal and negatively affecting sleep initiation and maintenance. Cognitive Behavioral Therapy for Insomnia (CBT-I) effectively addresses these issues by correcting maladaptive thought patterns (6,7).

Environmental Contributors: Poor sleep hygiene, such as inconsistent sleep routines and stimulant use, along with external factors like noise, temperature, and light, further impair sleep quality (8).

Outside Stimuli: Noise, light, and temperature also can have an effect on sleep exceptional and contribute to the improvement of insomnia (9).

Glutamatergic Activity: Hyperactive glutamatergic signaling in the brain contributes to insomnia through mitochondrial dysfunction, oxidative stress, and inflammation. This imbalance also

relates to anxiety disorders. mGlu2/3 receptors, involved in modulating glutamate levels, are concentrated in brain regions associated with anxiety, including the amygdala and hippocampus [10,11].

Cedarwood oil, extracted from the trees of Cedrus deodora or Juniperus virginiana, has been valued for its therapeutic properties. Derived from the wood of these trees, its composition varies based on factors such as the species of cedar, soil composition, climate, altitude, and cultivation practices. The primary components of cedarwood oil typically include cedrol, cedrene, and thujopsene, along with various sesquiterpenes and sesquiterpene alcohols. Cedarwood oil is known for its calming and grounding effects, insect-repelling properties, and anti-inflammatory and antiseptic properties. It is often used in aromatherapy to promote relaxation, reduce stress and anxiety, and improve sleep quality. [12,13].

Passionflower oil, derived from the seeds of the Passiflora species, commonly Passiflora incarnata, has also been highlighted for its capability in coping with insomnia. Native to tropical and subtropical regions of the Americas, passionflower flora are cultivated globally in appropriate climates. The composition of passionflower oil frequently carries a tremendous share of linoleic acid, an omega-6 fatty acid, in addition to oleic acid, palmitic acid, and stearic acid. Additionally, passionflower oil may additionally include various nutrients, consisting of vitamin E (tocopherols), and other bioactive compounds including flavonoids and alkaloids [14-16].

2. MATERIALS REQUIRED

Glass wares: Borosil and ASGI make glass wares were used.

Chemicals: Analytical grade chemicals including Tween 20, Oleic Acid, Propylene Glycol, NaOH, KOH, Silica Gel, Ethanol, Diazepam, TLC plates, and Distilled Water.

Animals: Wistar Albino rats (150–200 g, both sexes) were obtained from CPCSEA-registered breeders. Housed under controlled conditions (12-hour light/dark cycle, 25 ± 2°C), they received ad libitum access to food and water. The study followed CPCSEA ethical guidelines.

3. METHODS

Procurement of essential oils

Ceedarwood essential oil and passionflower essential oil was procured for experiment.

Standard drug: Diazepam tablet I.P Valium®5, Mfg.Lic No: MNB/06/295, Manufactured by Abbott Healthcare Pvt.Ltd were used as a standard drug

Preparation of microemulsion:

Oleic acid and Tween 20 were mixed in appropriate ratios. Essential oils were dissolved in this surfactant blend with mild agitation. Water was slowly added with continuous stirring to form a clear microemulsion. Sonication and heating were applied if necessary to facilitate emulsification. The mixture was stirred until it cooled to room temperature.

Phytochemical studies

Stock solution: 1g of the essential oil (Ceedarwood oil and Passion flower oil) were dissolved in 10 ml of ethanol to obtain 100mg/ml concentration.

Test of fatty acid

A few drops of phenolphthalein indicator should be added to the stock solution. Next, use the 0.1 N KOH solution to titrate, gradually adding KOH until the solution takes on a light pink hue that lasts for around 15 seconds. All of the free fatty acids have been neutralized, as indicated by this color shift.

Test for terpenoids

A tiny quantity of essential oils (passion flower and chamomile oil) sample was added to the bottom of a TLC plate using a capillary tube after a silica gel plate serving as the stationary phase was utilized. Till the bottom of the developing chamber was covered, a tiny amount of toluene was added.

Make sure the sample spot is above the solvent level by placing the spotted TLC plate into the development chamber. So that the solvent could move up the plate through capillary action, the developing chamber was covered to stop evaporation. The TLC plate was taken out of the developing chamber and dried once the solvent front achieved the height that was required. Fluorescent patches visible under ultraviolet light.

Test for flavonoids

The alkaline reagent test demonstrates the presence of flavanoids by producing a bright yellow hue when a drop of NaOH solution is added to a stock solution. This color goes colorless when a few drops of diluted acid are added.

Animals and drug treatment:

There were twenty rats in the study. Each of the five groups that they were split up into contained four rats. Group I acts as the lone recipient and is in charge. As a positive control, Diazepam (1 mg/kg, po) was administered to Group II.ME was administered to Groups III–V. The M.E. was ready on the day of the test.

Rotarod test: By Dunham and Miya (1957), Rotarod is explained.Mice's neuromuscular control is typically estimated using this method. In order to generate friction and keep mice from slipping off the rod, rotarods are often made of rods coated with polypropylene foam. A distance of roughly 15 cm separates the rod from the floor.With over study, the motor-driven rod may be kept at a constant speed of 20 rpm. Over the course of two days, three trials per day lasting two minutes each were conducted with the animals on a rotarod. Mice received an extract treatment on day three, both before and after.

Actophotometer: To monitor the locomotor activity of mice, an actophotometer is used. The animals were put inside an actophotometer, which contains light beams that are always on and that cross the chamber and land on photoelectrical cells that correspond. Every break in the recording that occurs when the mouse moves across the light beams was captured for ten minutes. Interruptions in the photo beam as a whole indicate the movement of mice. [27]

4. RESULT AND DISCUSSION:

Most commonly used to treat anxiety disorders and insomnia, the synthetic benzodiazepine class of medications also has a number of negative side effects, including tremor, disorientation, lethargy, depression, anterograde amnesia, disinhibition, and irritability. A patient's health may be seriously impacted by a common adverse effect or a severe one, such as respiratory depression, suicidality, seizures, bradycardia, cardiovascular collapse, syncope, etc.

Fortunately, natural medicinal plants are thought to provide an additional or alternate form of treatment for anxiety and insomnia that has fewer negative effects.

Extant research has demonstrated that the antioxidant content of essential oils is enhanced when they are combined, such as chamomile and passion flower essential oils. In the current trials, we are using a blend of essential oils rather than individual oils, as many prior studies have demonstrated the great effectiveness of plants with strong antioxidant qualities in treating anxiety disorders and sleeplessness

This qualitative chemical test indicates the presence of terpenoids, flavanoids, and fatty acids. Contributing to their sedative qualities include the presence of fatty acids, terpenoids, and flavanoids. For their ability to relax the central nervous system, these substances have been researched.

The current research use an actophometer and model rotarod to examine the pharmacological activity of essential oils including chamomile and passion flower for the treatment of insomnia.

Rotarod:

According to the aforementioned research, when compared to the control group, both diazepam and microemulsion cause the time it takes for rats to fall off the rod to be shorter. After applying the microemulsion, we saw that the rat's time falling off the rod decreased (Table 1), indicating that all microemulsions—individual and combined—possess considerable anti-insmonic activity. The highest anti-insmonic activity, however, was demonstrated by combination microemulsion.

Actophometer:

The aforementioned experiments demonstrate that, as compared to the control group, both diazepam and microemulsion cause a decrease in the locomotor activity of rats. Upon examining Table 2, we saw that the rats' locometry activity had decreased following the application of the microemulsion. This suggests that all microemulsions, whether single or combined, exhibit noteworthy anti-insmonic activity. Nevertheless, the highest anti-inflammatory efficacy was demonstrated by combination microemulsion.

Table 1: Results on rotarod

S.No.	Treatment	Dose	Time of animals remained without falling from rod(sec.)		
			30 min.	60min.	90min.
1.	Vehicle	Water	181.56 ±4.44	163.14±3.12	156.62±3.35
2.	Diazepam	1mg/kg	166.65±3.23	140.12±4.37**	109.56±2.15***
3.	Ceedarwood microemulsion	Transdermal application	157.21±1.34	145.87±2.35	145.12±2.29*

4.	Passionflower microemulsion	Transdermal application	165.45±2.68	163.83±1.89*	139.45±2.14**
5.	Combination microemulsion	Transdermal application	157.22±2.32	135.35±2.51**	116.04±3.50***

All values are mean ±SEM (n=4); *p< 0.05,** p<0.01,***p<0.001, when compared to control

Table 2: Results on actophometer

S.No.	Treatment	Dose	Locomotor activity (number of count)		
			Before dose Administration	After 30(min.)	After 60(min.)
1.	Vehicle	Water	250.51±2.20	255.31±2.18	247.54±2.70
2.	Diazepam	1mg/kg	258.05±3.18	225.04±3.26***	188.05±2.37***
3.	Ceedarwood microemulsion	Transdermal application	240.66±2.49	257.60±3.40	227.55±2.55***
4.	Passionflower microemulsion	Transdermal application	246.74±2.79	235.55±2.30***	217.50±2.84***
5.	Combination microemulsion	Transdermal application	256.77±3.14	228.05±2.68***	189.76±2.22***

All values are mean ±SEM (n=4); *p< 0.05, **p<0.01,***p<0.001 when compared to control

5. CONCLUSION

Our investigation indicates that microemulsions, especially those combining cedarwood and passionflower oils, demonstrate significant anti-insomnia activity. These results were comparable to diazepam and suggest the utility of such formulations for natural, safer insomnia treatment. The mechanism likely involves antioxidant and CNS-modulatory effects of active constituents. Future studies should focus on clinical validation and exploring long-term safety.

REFERENCES

[1] Buysse, D. J., Germain, A., Hall, M., Monk, T. H., & Nofzinger, E. A. (2011). A Neurobiological Model of Insomnia. Drug Discov Today Dis Models, 8(4), 129-137. doi: 10.1016/j.

[2] Kalmbach, D. A., Cuamatzi-Castelan, A. S., Tonnu, C. V., Tran, K. M., Anderson, J. R., Roth, T., & Drake, C. L. (2018). Hyperarousal and sleep reactivity in insomnia: current insights. Nat Sci Sleep, 10, 193-201. doi: 10.2147/NSS.S138823.

[3] Potter, G. D., Skene, D. J., Arendt, J., Cade, J. E., Grant, P. J., & Hardie, L. J. (2016). Circadian Rhythm and Sleep Disruption: Causes, Metabolic Consequences, and Countermeasures. Endocr Rev, 37(6), 584-608. doi: 10.1210/er.2016-1083.

[4] Fernandez-Mendoza, J., & Vgontzas, A. N. (2013). Insomnia and its impact on physical and mental health. Curr Psychiatry Rep, 15(12), 418. doi: 10.1007/s11920-013-0418-8.

[5] Rossman, J. (2019). Cognitive-Behavioral Therapy for Insomnia: An Effective and Underutilized Treatment for Insomnia. Am J Lifestyle Med, 13(6), 544-547. doi: 10.1177/1559827619867677.

[6] Bollu, P. C., & Kaur, H. (2019). Sleep Medicine: Insomnia and Sleep. Mo Med, 116(1), 68-75.

[7] Godos, J., Grosso, G., Castellano, S., Galvano, F., Caraci, F., & Ferri, R. (2021). Association between diet and sleep quality: A systematic review. Sleep Med Rev, 57, 101430. doi: 10.1016/j.smrv.2021.101430.

[8] Alloy, L. B., Labelle, D., Boland, E., Goldstein, K., Jenkins, A., Shapero, B., ... & Obraztsova, O. (2012). Mood disorders. In J. E. Maddux & B. A. Winstead (Eds.), Psychopathology: Foundations for a contemporary understanding (3rd ed., pp. 195–246). Routledge/Taylor & Francis Group.

[9] El Mihyaoui, A., Esteves da Silva, J. C. G., Charfi, S., Candela Castillo, M. E., Lamarti, A., & Arnao, M. B.

(2022). Chamomile (Matricaria chamomilla L.): A Review of Ethnomedicinal Use, Phytochemistry and Pharmacological Uses. Life (Basel), 12(4), 479. doi: 10.3390/life12040479.

[10] Tiwari, S., Singh, S., Tripathi, S., & Kumar, S. (2015). A Pharmacological Review: Passiflora Species. Asian J. Pharm. Res, 5(4), 195-202.

[11] Microemulsions: Current Trends in Novel Drug Delivery Systems. (2022). Journal of Pharmaceutical Negative Results, 13, 2327-2334.

[12] Santos, P., Watkinson, A. C., Hadgraft, J., & Lane, M. E. (2008). Application of microemulsions in dermal and transdermal drug delivery. Skin Pharmacol Physiol, 21(5), 246-259. doi: 10.1159/000140228.

[13] Jadhav, K. R., Shaikh, I. M., Ambade, K. W., & Kadam, V. J. (2006). Applications of Microemulsion Based Drug Delivery system. Curr. Drug Deliv, 3, 267-273.

[14] Talegaonkar, S., Azeem, A., Ahmad, F. J., Khar, R. K., Pathan, S. A., & Khan, Z. I. (2008). Microemulsions: a novel approach to enhanced drug delivery. Recent Pat Drug Deliv Formul, 2, 238-257.

[15] Eccleston, M. (2002). Emulsion and microemulsions. In J. Swarbrick & J. C. Boylan (Eds.), Encyclopedia of pharmaceutical technology (2nd ed., pp. 1080-1085). Marcel Dekker, Inc.

[16] Roberts, F., Harris, T. (2020). Passionflower Oil: A Review of Its Potential in Managing Insomnia. Herbal Medicine Today, 7(3), 150-165..