ORIGINAL ARTICLE

The interaction of Suk-Saiyasna remedy with GABAA and CB1 receptor-targeting drugs: Enhancing hypnotic and sedative effects in *in vivo* models

Watchara Damjuti, Worathat Thitikornpong[1,2], Sinsamut Saengow[3], Thanundorn Thanusuwannasak[4], Thanes Fuangfoo[5], Jurairat Boonruab[6]

Department of Integrative Medicine, Faculty of Integrative Medicine, Rajamangala University of Technology Thanyaburi, [3]Department of Animal Production Technology and Animal Health Science, Faculty of Agricultural Technology, Rajamangala University of Technology Thanyaburi, [5]Department of Pharmacology, College of Pharmacy, Rangsit University, [6]Department of Applied Thai Traditional Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, [1]Department of Food and Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn University, [2]Centre of Excellence in DNA Barcoding of Thai Medicinal Plants, Chulalongkorn University, [4]Chulalongkorn University Drugs and Health Product Innovation Promotion Centre, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand

J. Adv. Pharm. Technol. Res.

ABSTRACT

The Suk-Saiyasna remedy, an herbal treatment, was historically used but ceased due to its cannabis content. After a relaxation of drug control laws in Thailand, its use re-emerged. This study examines the Suk-Saiyasna remedy's impact on rodent behavior and its receptor effects. This study was conducted to assess the sedative-like effects of the remedy on mice. The mice were divided into groups receiving 0.6, 3, 30, and 60 mg/kg extracts, with negative controls for comparison. We also investigated the impact on receptors, utilizing negative controls and pretreatment with receptor blockers, followed by either a negative control or a 60 mg/kg extract. Furthermore, this study investigated the behavioral aspects of mice, including anxiolytic effects, antidepressant-like effects, and motor coordination, utilizing the elevated plus-maze, open-field, and rotarod performance tests. The Suk-Saiyasna remedy ($P < 0.05$) decreased significantly in the latent period and increased sleeping time in the treated groups. Moreover, the Suk-Saiyasna remedy also showed efficacy in reaction to GABAA receptors and cannabinoid CB1 receptors ($P < 0.05$). In addition, positive effects were observed regarding the animal behavior in the arena, as the animal activity, behavior, and muscle coordination were reduced ($P < 0.05$). The Suk-Saiyasna remedy may be involved in a sedative–hypnotic-like effect in rodents under normal conditions through the modulation of GABAergic neurons and induction of the cannabinoid CB1 receptor mechanism.

Key words: Hypnotic-like effect, sedative-like effect, sleep, Suk-Saiyasna, Thai traditional medicine

INTRODUCTION

Cannabis sativa L., known for psychoactive compounds like tetrahydrocannabinol (THC), has a centuries-old history, likely originating in central Asia or western China.[1] It was used for its healing properties as early as 2700 BC, documented in Emperor Shen Nung's pharmacopoeia.[2] Various civilizations, including Indian Hindus, Assyrians,

Address for correspondence:
Dr. Watchara Damjuti,
Department of Integrative Medicine, Faculty of Integrative Medicine, Rajamangala University of Technology Thanyaburi, Pathum Thani 12130, Thailand.
E-mail: watchara_d@rmutt.ac.th

Submitted: 08-Jul-2023 **Revised:** 02-Nov-2023
Accepted: 14-Nov-2023 **Published:** 15-Jan-2024

Access this article online

Quick Response Code:

Website: www.japtr.org

DOI: 10.4103/JAPTR.JAPTR_355_23

How to cite this article: Damjuti W, Thitikornpong W, Saengow S, Thanusuwannasak T, Fuangfoo T, Boonruab J. The interaction of Suk-Saiyasna remedy with GABAA and CB1 receptor-targeting drugs: Enhancing hypnotic and sedative effects in *in vivo* models. J Adv Pharm Technol Res 2024;15:13-8.

Greeks, Romans, and Thailand during King Narai's reign, historically employed cannabis for medicinal purposes. Concerns about addictiveness, arising from the 1961 Single Convention on Narcotic Drugs, led to a cessation of its use. In Thailand, the Narcotics Act, which has been in effect since 1922, experienced a revival in the use of medical cannabis oil, ultimately leading to the passage of the 2019 Narcotic Drugs Act (No. 7), which permits controlled medical use. The Department of Thai Traditional and Alternative Medicine collected historical cannabis-containing medicinal formulas, paving the way for Thai traditional medicine, although many formulations remain restricted due to rarity and CITES listing. In 2020, the Ministry of Public Health initiated specialized clinics with 16 pilot formulations operated by medical cannabis clinicians.[3]

The Suk-Saiyasna remedy, originating from the ancient Thai Thart Phra Narai Scripture, is part of 16 early medicinal cannabis formulations dating back to the pre-Sukhothai period (12th century).[4] It has a history of use for sleep, pain relief, and appetite stimulation, containing various herbal compounds. Despite its centuries-old tradition, its use was interrupted due to legal and public health changes. Recent changes in cannabis laws have rekindled its medical use, but limited research exists on such products, creating a gap in our understanding. To address this, our study investigates the Suk-Saiyasna remedy's pharmacological effects and mechanism of action related to sedation.

MATERIALS AND METHODS

Plant materials

The plant materials in this study were purchased from an herbal pharmacy that is registered with the Ministry of Public Health, Thailand. *C. sativa* leaves were purchased from a licensed community enterprise in Thailand. All plant materials were then identified and confirmed by a specialist from the Thai Traditional Pharmacy and Botanical Pharmacy division of the Faculty of Integrative Medicine, the Rajamangala University of Technology Thanyaburi (RMUTT) before the extraction procedures were started.

Drug extraction

Suk-Saiyasna remedies were formulated through consequently grinding and blending of camphor (25 g), *Azadirachta indica A. Juss.* Leaf (50 g), *Clausena excavate* BURM. f. wood (75 g), *Cinnamomum bejolghota* (Buch.-Ham.) Sweet bark (100 g), *Nigella sativa* L. fruit (125 g), *Aucklandia lappa* Dence root (150 g), *Myristica fragrans* Houtt. fruit (175 g), *Mesua ferrea* L. flower (200 g), *Piper nigrum* L. seed (225 g), *Zingiber officinale* Roscoe rhizome (250 g), *Piper retrofractum* Vahl fruit (275 g), and *C. sativa* L. leaf (300 g). The mixed powder was macerated in 80% ethanol until complete extraction. The resulting aqueous solution was filtered using Whatman number 1 filter paper, and then alcohol was removed through a rotary evaporator (Buchi, Switzerland). The resulting extract was further concentrated using cryodesiccation (Labconco Corporation, USA), yielding 13.38% w/w. The crude extract was preserved at −20°C for potential future utilization in the study.

Quantitative cannabis component based on the Suk-Saiyasna remedy

Chromatographic separation was carried out using a liquid chromatography-tandem mass spectrometry (LC–MS)/MS system (Shimadzu LCMS-8050 Triple Quadrupole Mass Spectrometer, Kyoto, Japan) with a Restek column. LC–MS grade mobile phase solvents were used. Standards of cannabidiol and Δ-9-THC were prepared at a stock concentration of 1000 ppb and then diluted in a 25:75 LC-MS grade water: Methanol mixture to create a concentration range from 1 to 2000 ng/mL. For quantification, samples were further diluted with ethanol and analyzed using a Shimadzu Nexera UHPLC with LCMS-8050 under the following conditions: 40°C column temperature, 5 µL injection volume for HPLC, heated ESI ionization, and gas flow rates of 3 L/min nebulizing gas, 10 L/min drying gas, 10 L/min heating gas, with DL temperature set at 250°C, heat block temperature at 400°C, and interface temperature at 370°C for the LCMS-8050 Triple Quad Mass Spectrometer.

Animals

Male ICR mice (age: 2 months, weight: 22 ± 2 g) were obtained from the National Laboratory Animal Centre at Mahidol University, Thailand. A total of 192 mice were housed in groups of up to four per cage under controlled conditions (25°C ± 2°C, 40%–60% humidity) with a 12-h light/dark cycle (lights on at 6 AM). They had unrestricted access to food and water and underwent a 1-week adaptation period in the same colony before experiments. All experiments adhered to daytime protocols and followed animal care guidelines specified by the National Research Council of Thailand, as well as approved protocols by the Institutional Animal Ethics and Care Review Board of (RMUTT. TMC.2019.R001).

Benzodiazepine-induced sleeping time test

The evaluation of benzodiazepine-induced sleep duration followed a modified protocol from previous literature.[5] In this study, nine groups, each comprising eight mice, were formed. Group I, the negative control received sterile water. Groups II to V received oral doses of the extract at concentrations of 0.6, 3, 30, and 60 mg/kg, respectively. Groups VI and VII received pretreatment with 3.5 mg/kg flumazenil (dissolved in 10% dimethyl sulfoxide) before being administered the 60 mg/kg extract, while the negative control group followed the same procedure. Groups VIII and IX received a preliminary treatment of 0.1 mg/kg rimonabant (dissolved in 10% dimethyl sulfoxide) from Tokyo Chemical Industry Co., Ltd., Japan, followed by the administration of the 60 mg/kg extract

and the negative control. The extracts, suspended in sterile water, were administered orally through gavage. Sleep was induced intraperitoneally in the animals with diazepam (30 mg/kg; GPO, Thailand) 30 min following oral extract administration. The duration it took for the animals to enter sleep and the overall duration of their sleep were observed and contrasted with the control group, using the righting reflex as a benchmark.[6,7]

Elevated plus-maze test

The elevated plus-maze (EPM) test, a common model for assessing rodent anxiety-related behaviors, was employed in this study.[8,9] Eight mice were assigned to each of the five groups. Group I received sterile water (negative control), while Groups II, III, IV, and V were administered oral doses of 0.6, 3, 30, and 60 mg/kg of the extract by gavage. The trials took place in a dimly lit room (30 lux white light in the maze center) 30 min after administration. Locomotor activity was evaluated using the total entries into open and closed arms. Video recordings of EPM exploration were analyzed for time spent in open and closed arms and total arm entries, with ethnological analyses based on the initial 5 min of exploration.[10] The testing environment was regularly cleaned and dried.

Open-field test

The open-field test was conducted following established protocols, ensuring consistency with the experimental groups and feeding methods described in prior studies.[11] Afterward, the mice were placed at the center of the apparatus, and their behaviors were monitored for 5 min, beginning half an hour after the treatment. The total of center entries and behaviors was utilized to assess their locomotor activity.[12] Various behaviors, such as moving across lines, entering the central square, stretching, defecation, urination, standing on hind legs, and performing grooming actions such as face rubbing, licking paws, grooming fur, and head scraping were meticulously observed and documented.

Rotarod performance test

Motor coordination was assessed using the Rota Rod apparatus (Model 76–0770, Harvard Apparatus, USA), with consistent experimental groups and feeding protocols. Thirty minutes after gavage, mice were placed on a rotating horizontal metal rod (3 cm diameter, 10 rpm/min), and their balance time was recorded. Each mouse had two trials, lasting up to 300 s, with a 30–60-min rest between trials. The test area was cleaned with odorless wet tissue paper and dried after each use.

Data analysis and statistics

Data were collected, recorded in a spreadsheet, and subsequently analyzed. Descriptive statistics were computed, and the results are presented as mean ± standard deviation. The mean comparison was performed using one-way ANOVA with Dunnett's *post hoc* at a 95% confidence level with $P < 0.05$. Statistical analysis was conducted using IBM SPSS 23.0 (Armonk, NY, USA) software, and findings are visualized through tables and graphs.

RESULTS

Quantitative cannabis component based on the Suk-Saiyasna remedy

The LC–MS/MS results revealed that this remedy possesses bio compounds such as cannabidiol and Δ-9-THC [Table 1].

Sedation-like effect of Suk-Saiyasna remedy by the benzodiazepine-induced sleeping time test

Male albino ICR mice (n = 8 per group) received a single forced-fed dose of the Suk-Saiyasna remedy followed by simultaneous benzodiazepine exposure. The period from awakening to the onset of sleep was notably extended, and the duration of sleep was lengthened in comparison to the negative control group [Figure 1]. The study also investigated the effects of psychotropic drugs on the GABAA and CB1 receptors. Mice pretreated with 3.5 mg/kg flumazenil followed by the extract and diazepam showed a reflex onset time of 6.03 ± 1.26 min and sleep duration of 115.83 ± 10.59 min ($P < 0.05$). Mice pretreated with 0.1 mg/kg rimonabant followed by the extract and diazepam demonstrated a reflex onset time of 3.15 ± 0.19 min and a sleep duration of 92.25 ± 4.86 min ($P < 0.05$) [Table 2].

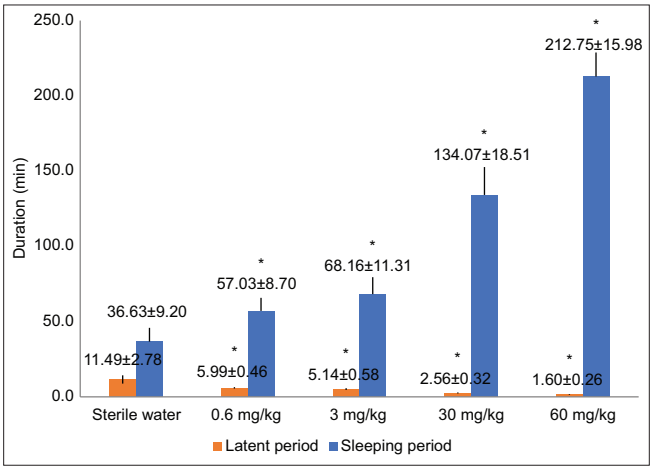

Figure 1: The Suk Saiyasna remedy's impact on latency and sleep duration in the benzodiazepine induced sleeping test. Data is expressed as mean ± standard deviation. *Significant difference ($P < 0.05$), Dunnett's test

Table 1: Quantitative cannabis component based on the Suk-Saiyasna remedy

Compound	Molecular formula	Suk-Saiyasna remedy (mg/g)
Cannabidiol	$C_{21}H_{30}O_2$	0.17
Δ-9-tetrahydrocannabinol	$C_{21}H_{30}O_2$	2.51

Sedative hypnotics-like effects

The Suk-Saiyasna remedy was assessed for its sedative hypnotic-like effects using the aforementioned methods. On the EPM, the remedy at different doses notably prolonged the duration spent in enclosed arms while reducing the time in open arms when compared to the negative control group ($P < 0.05$) [Figures 2 and 3]. In the open-field test, all remedy doses led to significantly fewer line crossings, center square entries, and reduced behaviors such as rearing, grooming, and stretch posture defecation (except urination) ($P < 0.05$). The rotarod test, assessing endurance, revealed that all remedy doses significantly reduced the time spent on the spinning rod compared to the negative control group ($P < 0.05$) [Table 3].

DISCUSSION

In this study, cannabinoid content in the Suk-Saiyasna remedy was quantified using LC–MS/MS, with the cannabidiol and Δ-9-THC doses calculated as 0.17 and 2.51 mg/g, respectively. Our investigation into the sedative

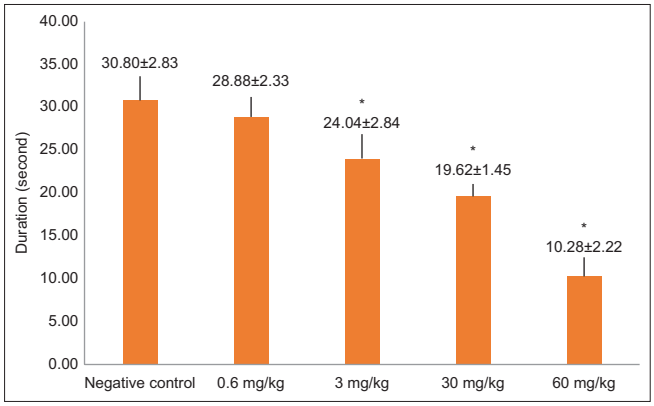

Figure 2: Effect of Suk-Saiyasna remedy on rodents' time in the open maze arm (mean ± standard deviation). *Significant difference ($P < 0.05$), Dunnett's test

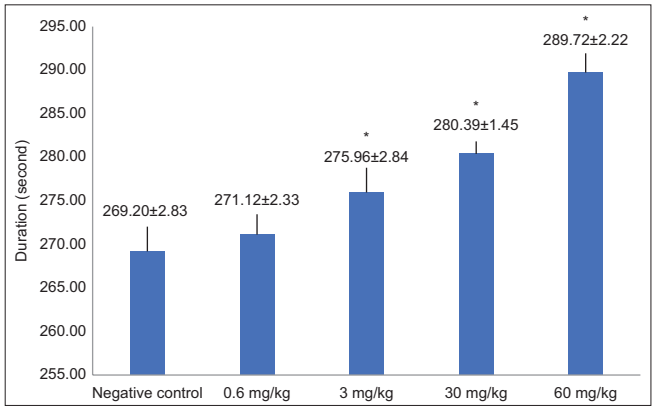

Figure 3: Effect of Suk-Saiyasna remedy on rodents' time in the closed maze arm (mean ± standard deviation). *Significant difference ($P < 0.05$), Dunnett's test

Table 2: Sedation-like effect of the Suk-Saiyasna remedy by benzodiazepine-induced sleeping time test in mice

Group	Pretreated	Intervention	Outcome	
			Latent time	Sleeping time
1	-	Sterile water	11.49±2.78	36.63±9.20
2	-	0.6 mg/kg extract	5.99±0.46*	57.03±8.70*
3	-	3 mg/kg extract	5.14±0.58*	68.16±11.31*
4	-	30 mg/kg extract	2.56±0.32*	134.07±18.51*
5	-	60 mg/kg extract	1.60±0.26*	212.75±15.98*
6	Flumazenil	60 mg/kg extract	6.03±1.26*	115.83±10.59*
7	Flumazenil	Sterile water	0.00±0.00	0.00±0.00
8	Rimonabant	60 mg/kg extract	3.15±0.19*	129.25±4.86*
9	Rimonabant	Sterile water	2.38±0.11	96.25±7.50

*Significant difference ($P<0.05$), determined by Dunnett's test. Data are presented as mean±SD. SD: Standard deviation

Table 3: Effects of the Suk-Saiyasna remedy on mouse muscle coordination and behaviors

Dosing	Rotarod performance test Duration (s)	Open field test						
		Time (*n*)		Behavior (*n*)				
		Line crossing	Center square entries	Rearing	Leaning	Grooming	Defecation	Urination
Sterile water	280.58±16.39	231.28±14.23	3.67±0.58	12.33±2.52	37.67±1.53	6.33±1.53	4.33±1.53	1.10±1.73
0.6 mg/kg	188.78±4.14*	134.88±11.80*	6.00±1.00	11.00±2.65*	36.00±3.00	4.67±0.58*	0.67±1.15	0.00
3 mg/kg	149.85±13.69*	54.75±6.86*	3.33±0.58*	8.67±0.58*	32.33±2.52*	3.44±1.53*	0.00*	0.00
30 mg/kg	88.58±12.43*	1.88±2.64*	0.00*	0.00*	0.00*	0.00*	0.00*	0.00
60 mg/kg	8.25±11.01*	1.50±2.14*	0.00*	0.00*	0.00*	0.00*	0.00*	0.00

*Significant difference ($P<0.05$), determined by Dunnett's test. Data are expressed as the mean±SD. SD: Standard deviation

and hypnotic effects of the remedy in *in vivo* models revealed its engagement of GABAA receptors, particularly the flumazenil-insensitive benzodiazepine binding sites, contributing to benzodiazepine-induced immobility. In addition, the remedy acted on the cannabinoid CB1 receptor, a key player in sleep induction.[13] We found that the remedy significantly reduced sleep onset time and extended sleep duration, indicating an impact on both cannabinoid GABAA and CB1 receptors. Altered animal behaviors were observed, suggestive of their influence on sedative and hypnotic effects. Sedatives, with various mechanisms of action, generally enhance gamma-aminobutyric acid (GABA) activity for stress alleviation and relaxation.[14] In our study, we noted a dose-dependent correlation between the administered benzodiazepine dose and the time to enter the latent phase. Lower doses had a minor effect, while higher doses significantly shortened the latent period, possibly indicating nonspecific neurotransmitter binding by the extract in the experimental group. To measure sleep duration, timing was assessed 30 min after treatment, followed by the administration of benzodiazepines. The duration from the onset of the righting reflex until its loss significantly increased [Table 2]. This might be attributed to the extract's receptor binding, which induced Cl − efflux, suppressing neurons and fostering a sedative-like effect.[15] To probe the drug's mechanism, flumazenil was employed to inhibit GABA neurons, delaying the latency period in comparison to the negative control. This suggests the Suk-Saiyasna remedy's potential to induce sedative effects or promote sleep by interacting with the GABAA receptor. In addition, we also employed rimonabant, a selective CB1 receptor blocker and inverse agonist. Although initially characterized as a CB1 receptor antagonist, rimonabant was subsequently discovered to also function as a mu-opioid receptor antagonist.[16] The CB1 receptor is associated with anxiolytic and sedative effects. Our results demonstrate that the Suk-Saiyasna remedy significantly reduced sleep onset time in animals pretreated with rimonabant and given 60 mg/kg of the extract. This indicates an interaction between the remedy and the CB1 receptor, resulting in shorter sleep onset times and prolonged sleep durations.

The behavioral and muscle coordination results align with the Suk-Saiyasna remedy's anxiolytic and sedative-like effects. The open-field test measures locomotor activity, anxiety, and exploratory tendencies in animals, given their natural aversion to well-lit open spaces. Increased exploration correlates with reduced anxiety levels, while anxiolytic and sedative-like effects lead to decreased mobility and alertness.[17] The open field is a confined space to prevent animal escape, marked with a grid and square crossings. Behavior studies followed established protocols.[18,19] Dose-dependent effects on animal behavior were observed, particularly pronounced at higher Suk-Saiyasna remedy concentration, with reduced grid line crossings and center square time. The lowest dose had milder effects, reducing time spent in the center of the test arena. Other behavioral measures indicated reduced rearing, grooming, defecation, and urination, reflecting the remedy's anxiolytic and sedative-like properties.[20] In the rotarod performance test, a dose-dependent decrease in balance ability was observed with higher extract doses, as indicated in Table 3. In the EPM test, animals spent more time in the closed arm compared to the open arm, consistent with previous findings on cannabinoids inducing anxiety-like responses.[21] Our study concurs with prior research on cannabinoids in the Suk-Saiyasna remedy, which may produce pronounced anxiety-like symptoms. In addition, it aligns with findings on cannabidiol and Δ-9-THC inducing hypo-locomotive effects and behavior interactions.[22]

CONCLUSIONS

The Suk-Saiyasna remedy potentiates a sedative and hypnotic-like effect in rodents under normal conditions and may modulate GABAergic neurons as well as induce the cannabinoid CB1 receptor mechanism. However, further studies are needed to determine the efficacy or insight mechanism of the drug and in either the acute or chronic toxicity testing.

Acknowledgments
We would like to acknowledge the support provided by the Thai Traditional Medical Knowledge Fund (Grant 6/2564) from the Department of Thai Traditional and Alternative Medicine, Ministry of Public Health. Our work is dedicated to the memory of the late and esteemed Associate Professor Nijsiri Ruangrungsi from Chulalongkorn University, whose inspiration guided our experiments.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Li HL. The origin and use of cannabis in eastern asia linguistic-cultural implications. Econ Bot 1974;28:293-301.
2. Zuardi AW. History of cannabis as a medicine: A review. Braz J Psychiatry 2006;28:153-7.
3. Ministry of Public Health. Announcement of the Ministry of Public Health: Prescribing Formulas for Narcotics of Category V Containing Cannabis Containing Compounds that can be Consumed for Medicinal Purposes or Research Studies. Gov Gaz 2020;136:27.
4. Office of Information and Evaluation; Ministry of Public Health, Department for Development of Thai Traditional and Alternative Medicine. Thai Traditional and Alternative Health Profile: Thai Traditional Medicine, Indigenous Medicine and Alternative Medicine, 2011–2013. Nonthaburi (Thailand): Ministry of Public Health; 2014.

5. Hafiz W, Zilani MN, Sultana NA, Isalm MM, Anisuzzman M, Hossain MG. Neuropharmacological potential of ceriscoides turgida (roxb.) leaf and root in mice. Clin Phytoscience 2019;5:1-6.
6. File SE, Pellow S. The effects of PK 11195, a ligand for benzodiazepine binding sites, in animal tests of anxiety and stress. Pharmacol Biochem Behav 1985;23:737-41.
7. Gao S, Calderon DP. Robust alternative to the righting reflex to assess arousal in rodents. Sci Rep 2020;10:20280.
8. Schneider P, Ho YJ, Spanagel R, Pawlak CR. A novel elevated plus-maze procedure to avoid the one-trial tolerance problem. Front Behav Neurosci 2011;5:43.
9. Komada M, Takao K, Miyakawa T. Elevated plus maze for mice. J Vis Exp 2008;22:1088.
10. Slikker W, Paule MG, Wang C. Handbook of Developmental Neurotoxicology. London, United Kingdom: Academic Press, An Imprint of Elsevier; 2018.
11. Seibenhener ML, Wooten MC. Use of the open field maze to measure locomotor and anxiety like behavior in mice. J Vis Exp 2015;96:e52434.
12. Sestakova N, Puzserova A, Kluknavsky M, Bernatova I. Determination of motor activity and anxiety-related behaviour in rodents: Methodological aspects and role of nitric oxide. Interdiscip Toxicol 2013;6:126-35.
13. Low ZX, Lee XR, Soga T, Goh BH, Alex D, Kumari Y. Cannabinoids: Emerging sleep modulator. Biomed Pharmacother 2023;165:115102.
14. Hepsomali P, Groeger JA, Nishihira J, Scholey A. Effects of oral gamma-aminobutyric acid (gaba) administration on stress and sleep in humans: A systematic review. Front Neurosci 2020;14:923.
15. Liu L, Jia S, Dong J, Zhang Y, Xu R, Zhang J. Sedative-hypnotic effect of YZG-330 and its effect on chloride influx in mouse brain cortical cells. Acta Pharm Sin B 2013;3:234-38.
16. Seely KA, Brents LK, Franks LN, Rajasekaran M, Zimmerman SM, Fantegrossi WE, *et al*. AM-251 and rimonabant act as direct antagonists at mu-opioid receptors: Implications for opioid/cannabinoid interaction studies. Neuropharmacology 2012;63:905-15.
17. de Sousa DP, de Almeida Soares Hocayen P, Andrade LN, Andreatini R. A systematic review of the anxiolytic-like effects of essential oils in animal models. Molecules 2015;20:18620-60.
18. Crusio WE. Genetic dissection of mouse exploratory behaviour. Behav Brain Res 2001;125:127-32.
19. Sturman O, Germain PL, Bohacek J. Exploratory rearing: A context- and stress-sensitive behavior recorded in the open-field test. Stress 2018;21:443-52.
20. Cryan JF, Sweeney FF. The age of anxiety: Role of animal models of anxiolytic action in drug discovery. Br J Pharmacol 2011;164:1129-61.
21. Haller J. Anxiety modulation by cannabinoids-the role of stress responses and coping. Int J Mol Sci 2023;24:15777.
22. Razmara P, Zaveri D, Thannhauser M, Ali DW. Acute effect of Δ-9-tetrahydrocannabinol on neuromuscular transmission and locomotive behaviors in larval zebrafish. J Neurophysiol 2023;129:833-42.