RESEARCH ARTICLE

pISSN: 0126-074X | eISSN: 2338-6223
https://doi.org/10.15395/mkb.v57.3919
Majalah Kedokteran Bandung. 2025;57(2):128–135

Majalah Kedokteran Bandung (MKB)

Received: April 5, 2024
Accepted: November 18, 2024
Available online: June 30, 2025

Acute Toxicity (LD_{50} value) of Peppermint (Mentha piperita) Suspension in Female Mice

Andriyanto,[1] Sharon Aurellia,[2] Muhammad Farhan Ibnu Hibban,[2] Tengku Zylviana,[2] Hamdika Yendri Putra[3]

[1]Division of Pharmacology and Toxicology, School of Veterinary Medicine and Biomedicine, IPB University, Bogor, Indonesia

[2]Students of Undergraduate Program, School of Veterinary Medicine and Biomedicine, IPB University, Bogor, Indonesia

[3]eLRosa Laboratory iRATco Group, Dramaga, Bogor, Indonesia

Abstract

Peppermint has several benefits, such as antibacterial, anti-inflammatory, and antifungal properties, that leads to its use in various products, especially in herbal medicine. This study aimed to evaluate the LD50 value of peppermint suspension through an acute toxicity test. This study was conducted at the Animal Laboratory Management Unit of the School of Veterinary Medicine and Biomedical Sciences, IPB University, from October 9 to 30, 2024. A total of 25 female mice were divided into 5 groups, and given different doses of peppermint suspension of 0, 0.5, 1, 1.5, and 2.0 g/kgBW. Observations were then carried out for 14 days on the parameters of body weight, physiological responses, clinical symptoms, absolute and relative organ weight, body weight, and number of mortalities per day. Results showed that the highest mortality was found in the groups administered with a 1.5 and 2.0 g/kgBW of peppermint suspension. Clinical symptoms, such as hair standing, lethargies, and decreased locomotor activity were also observed in these groups. In addition, the administration of peppermint suspension in mice had no significant effect on body weight, as well as on absolute and relative organ weight, It was also demonstrated that organs collected did not present any significant lesion. Thus, the acute toxicity test of peppermint suspension showed no macroscopic lesion or changes in organs and body weight. The LD50 value suggested that the is in the moderate toxicity category, with an LD50 value of 1.92 g/kgBW.

Keywords: Acute toxicity, alternative medicine, herbal extract, mice, peppermint

Introduction

Indonesia is a country abundant in natural resources, including medicinal plants. It is estimated that over 30,000 plant species exist in the country, with approximately 7,000 identified as medicinal.[1] The benefits of these medicinal plants have been studied, used in daily lives, inherited by the ancestors, and preserved by the community. In addition, various studies are competing to prove their efficacy, leading to the high potential of the herbal medicine industry. One of the medicinal plants that is often used in the industry is peppermint leaves.

Corresponding Author:
Andriyanto
Division of Pharmacology and Toxicology, Department Physiology and Pharmacology, School of Veterinary and Biomedical Sciences, IPB University, Bogor, Indonesia
Email: andriyanto@apps.ipb.ac.id

Peppermint plant belongs to the Lamiaceae family, which has approximately 30 species and various hybrids. It generally grows in sub-tropical areas,[2] and the leaves are recognized for their antineoplastic, antibacterial, anti-inflammatory, antiallergic, antifungal, antihepatotoxic, antiviral, antiradiation, and antinociceptive properties.[3] The main components of peppermint identified through hydro distillation are menthol (45.34%), menthone (16.04%), menthofuran (8.91%), cis-carane (8.70%), 1,8-cineole (4.46%), neo-menthol (4.24%), and limonene (2.22%).[4] These components give a soothing aroma, cool taste, and a variety of benefits for the body, leading to the wide use of the leaves in commercial medicines, toothpaste, aromatherapy, and food and beverage flavors. Peppermint has also been commonly used in some certain regions of Indonesia as an addition to herbal medicine.

Several studies have examined the benefits

of using peppermint, with some reporting that taking 40 drops of commercial peppermint extract in complementary medicine can improve nausea, vomiting, and anorexia in breast cancer patients undergoing chemotherapy.[5] Although peppermint leaves have many benefits for the body, their usage needs to be limited. The high menthol component causes side effects when consumed in excessive amounts, including agitation, dizziness, ataxia, hallucinations, seizures, and coma.[6] An acute toxicity test can be conducted to test the safety limit of consuming peppermint leaves to ensure that any consumable preparations made using mint use the safety limit as a reference. This test has the potential to identify the toxic effects of a preparation in a short period and is given through the oral route. Previous studies had been conducted regarding the toxicity limit of peppermint, such as Malekmohammad et al.[7] who observed the toxic effect of peppermint essential oil on mice, humans, insects, and rabbits. A study conducted by Yousuf et al.[8] also observed the acute oral toxicity of Japanese mint oil towards brine shrimp. Despite the existing literature, none has examined the LD_{50} of peppermint extract suspension on mice, along with observation of macroscopic organ lesion, organ weights, or body weight changes. Therefore, this study aims to determine the LD_{50} value and the effect of peppermint suspension on organ weight, macroscopic organ lesions, and body weight in female mice.

Methods

This study was approved by the Animal Ethics Commission of the School of Veterinary Medicine and Biomedicine, IPB University, with approval number 098/KEH/SKE/VIII/2023. The research was conducted at theAnimal Laboratory Management Unit, School of Veterinary Medicine and Biomedical Sciences, IPB University, from October 9 to October 30, 2023

The tools used in this study were 5 mice cages made of plastic, with dimensions of 35 cm, 25 cm, 10 cm, wire cover cages, using wood shavings as bedding. Each cage was set with a drinking bottle of 80 mL, digital scales, syringes, micropipettes with a capacity of 0 to 100 µ, digital thermogenic, and minor surgical tools. The materials used were commercially dried peppermint leaves obtained from Gubuk Herbal, Solo Regency, Indonesia, distilled water, and 25 *Deutschland Denken Yoken* (DDY) female mice weighing 20 to 30 g. Ivermectin was administered as an anthelmintic for 7 days in a row during acclimatization to ensure that the mice were free from any parasite infestations, preventing any potential interference with the study parameters.

Preparation for the peppermint suspension was performed by boiling 500 grams of dried peppermint leaves in 1000 mL of water until a full boil was reached, then maintaining the boil for 15 minutes. Subsequently, the dried peppermint leaves were filtered using a strainer.

The preparation of experimental animals and cages began with the acclimatization process. In this study, the initial stage started with cleaning the cage and preparing the tools that were used during the treatment period. The animals were acclimatized for 7 days to ensure that the mice could adapt to the new cage conditions and reduce the possible stress level. During the acclimatization process, mice were fed with 10% of their body weight and provided with ad libitum drinking water. Anthelmintic preparations were administered, which was ivermectin (0.04 mg/kg, diluted with distilled water), once a day for 7 days. Replacement of cage bedding in the form of wood shavings was done every 7 days.

This study was designed according to the Completely Randomized Design (CRD) method. An acute toxicity study was performed according to the method described by BPOM (2020), with modifications. The mice were separated into 5 groups based on the dosage administered. Each group contained 5 mice, with a negative control group and treatment groups administered with peppermint suspension in the dosage of 0.5, 1, 1.5, and 2.0 g/kgBW, respectively. The volume administered were 0.03, 0.06, 0.09, and 0,12 mL, respectively. Treatment was conducted by administering dried peppermint leaves suspension, which was purchased commercially and prepared by boiling it in water. Furthermore, the peppermint suspension was administered only once on the first day.

Observations during the study were performed every day after treatment on day 0 until the next 14 days. Parameters used for observation comprised the body weight, physiological response, clinical symptoms, absolute and relative organ weight, and the number of mortalities per day. Clinical symptoms observed included behavior, appetite and drinking, defecation, urination, hypersalivation, tremors, convulsions, and paralysis. Furthermore, physiological responses observed were body temperature, respiration

rate, and heart rate rate. Body weight weighing of mice was conducted once every 7 days, on days 0, 7, and 14 post-treatments. The experimental parameter to determine the value of LD_{50} in the acute toxicity test was to observe the number of mortalities of mice in each group from day 0 to day 14. Mice that died was later dissected for organ collection and weighing. Mice that were still alive until day 14 were euthanized by the cervical dislocation method. Subsequently, the removal of organs in the body (liver, innards, kidneys, lungs, heart, spleen) was performed for macroscopic observation of the organs and organ weighing using digital scales. The relative weight of the organ was obtained by the dividing value of the absolute weight of the organ by the body weight of the mice on the last day of observation and then multiplied by 100%.[10] The organs were also examined macroscopically for any signs of abnormalities.

Data were analyzed using Kruskall-Walli's method from the Minitab 19 software and the value of LD_{50} was measured using Probit analysis. The probit model assumed that the relationship between the independent variables and the probability of the outcome was determined by the Cumulative Distribution Function (CDF) of the normal distribution. This was different from logistic regression, which used the logistic (sigmoid) function. The data from the analysis and LD_{50} value could be interpreted to continue the discussion of the study results.

Results

The major parameter observed in acute toxicity testing (LD_{50}) to determine the toxicity level of the peppermint suspension was the percentage of mortality or death.[11] Mortality rate was analyzed from the day of peppermint suspension administration to day 14 using the probit analysis method. Mortality was observed at the dosage of 2.0 g/kg BW on day 3 and at the dosage of 1.5 g/kg BW on day 10. The result of the analysis of the LD_{50} value of peppermint suspension obtained using the probit analysis method was 1.92 g/kg BW. The mortality rate of mice at several dosages of peppermint suspension was presented in Table 1.

Observation of clinical symptoms in mice was routinely monitored once in a day at the same hour for 14 days after the administration of peppermint suspension. Based on qualitative observations, abnormal clinical symptoms were found in several mice, such as in the mice administered with dosages of 1.5 and 2.0 g/kgBW. The clinical symptoms shown by several mice were symptoms of depression, hair standing, lethargies, and decreased locomotor activity.

Other parameters observed were physiological responses and the body weight of the mice. Physiological responses observed were heart rate, respiratory rate, and temperature, which were observed routinely once a day at the same hour, starting from day 0 to day 14, while body weight weighing was conducted on days 0, 7, and 14 after mint suspension administration. The results of data analysis of body weight and physiological responses of mice were displayed in Figure 1.

Based on Figure 1, the results of the analysis of the average body weight using Kruskall-Wallis's method did not indicate any significant differences in the administration of peppermint suspension in various doses compared to the control (A). This proved that the administration of mint suspension did not affect the body weight of mice.

In this study, the parameter of heart rate was shown in Figure 1. The average results of heart rate were in a fluctuating range, which was 86 to 216 ×/minute (B and the average respiratory rate was also fluctuating, and was in the range of 82-147 ×/minute (C). Furthermore, the average

Table 1 Relationship Between Peppermint Suspension Dosage and Mortality Rate in Mice

Peppermint Suspension Dosages (g/kgBW)	Number of Mice	Number of Mortalities	Day of Mortality	Mortality Rate (%)
0	5	0	-	0
0.5	5	0	-	0
1	5	0	-	0
1.5	5	1	10	20
2	5	1	3	20

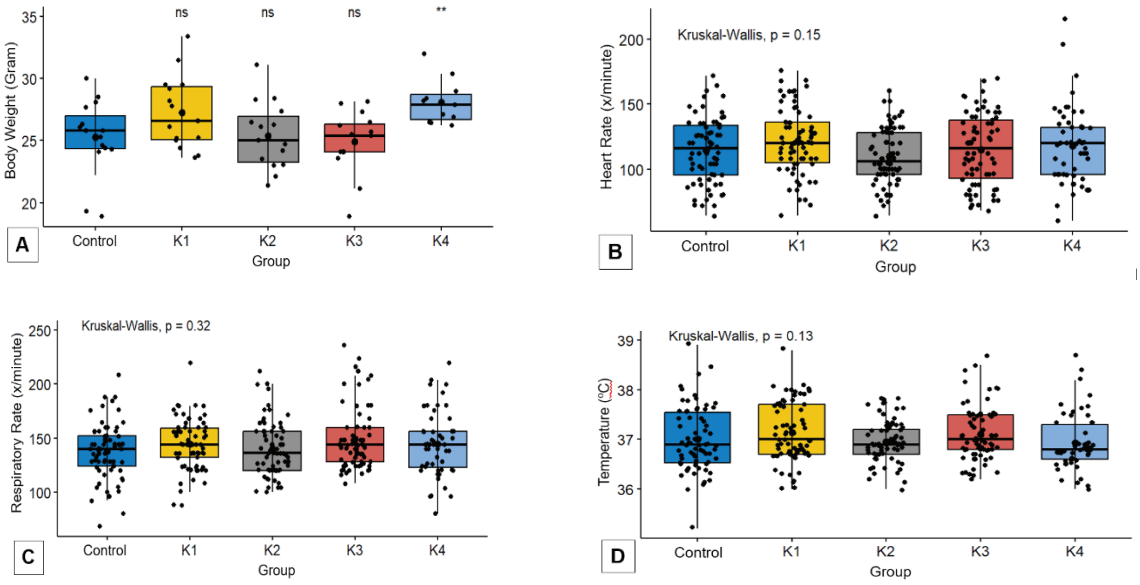

Figure 1 Peppermint Suspension Effect on Body Weight and Physiological Responses of Mice

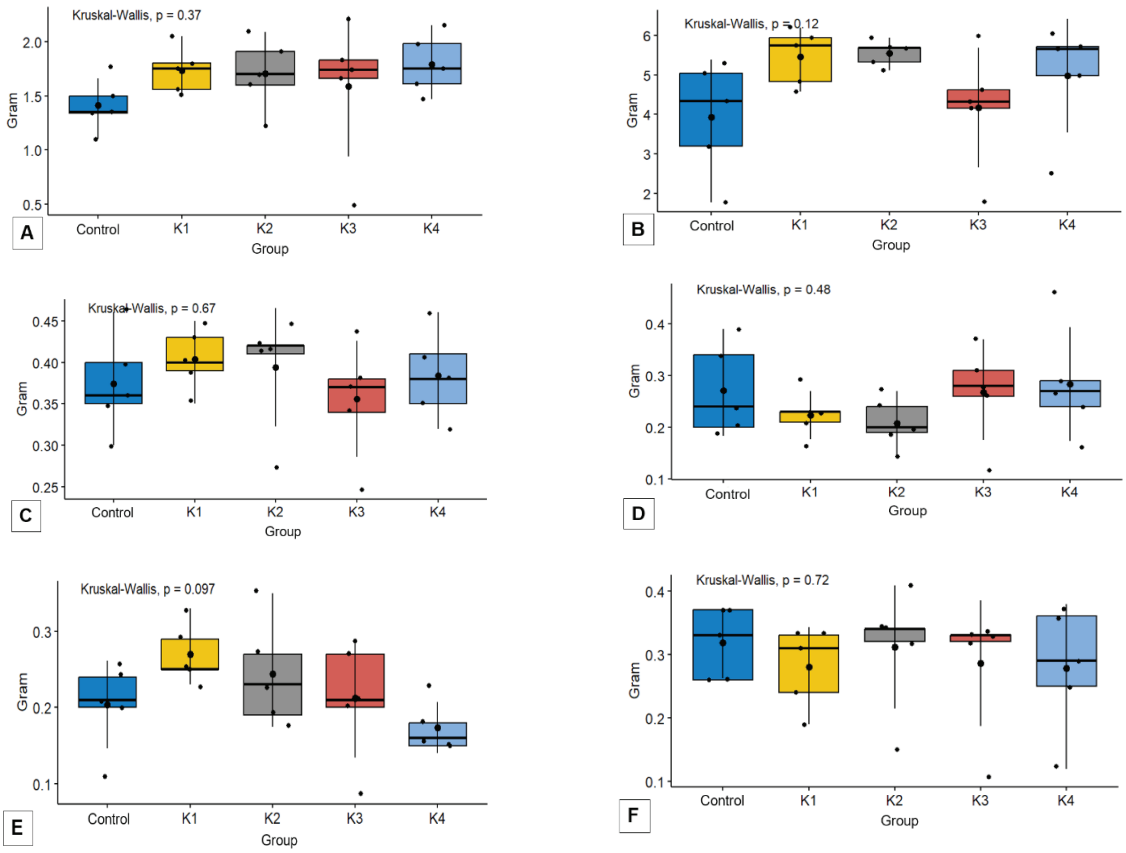

Figure 2 Effect of Peppermint Suspension on Absolute Organ Weights of Mice
(A) Liver; (B) Intestines; (C) Kidneys; (D) Lungs; (E) Heart; (F) Spleen

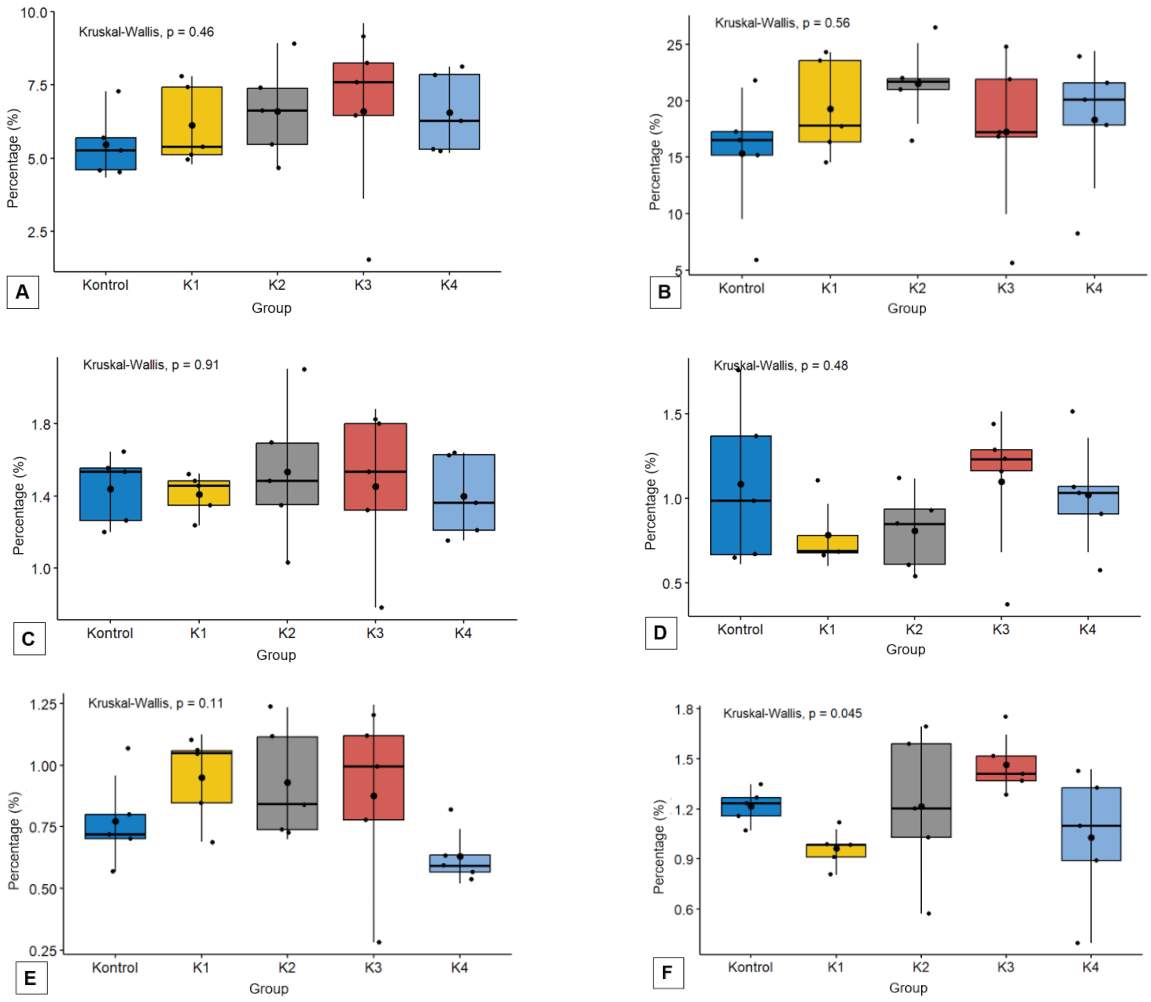

Figure 3 Effect of Peppermint Suspensionon Relative Organ Weights of Mice (A) Liver, (B) Innards (C) Kidneys (D) Lungs (E) Heart (F) Spleen

temperature results were in the range of 36.3 to 38.5°C (D). The average heart rate, respiration rate, and temperature of mice for 14 days since the administration did not reveal any significant difference between mice administered with peppermint suspension in various dosages compared to the control. This proved that peppermint suspension did not influence the physiological responses of mice in the form of heart rate, respiratory rate, and temperature observed.

Macroscopic observation of the organs indicated that all organs were normal in color, with the heart, liver, and spleen showing a reddish-brown color, the innards showing a pinkish-pale color, and the lungs showing a pale pink color. No lesions, nodules, hemorrhage, or fatty deposits were observed.

According to Figure 2, there was no significant difference found in the absolute weight parameters of liver (A), innards (B), kidneys (C), lungs (D), heart (E), and spleen (F) between mice administered with peppermint suspension at various dosages and control. This proved that the administration of mint preparations at doses of 0.5, 1, 1.5, and 2.0 g/kg BW did not affect the absolute organ weight.

Similarly, Figure 3 shows that the relative weights of the same organs did not significantly differ across treatment groups. These findings support the conclusion that peppermint suspension, at doses up to 2.0 g/kg BW, did not affect relative organ weight.

Discussion

Peppermint was one of the traditional herbal plants that was widely used in Indonesia[9], it had a high menthol content, which accelerated circulation, and relieved bloating, nausea, and cramps. Furthermore, peppermint also exhibited secondary metabolite compounds, namely tannins and flavonoids, which were believed to accelerate the digestive system.[10,11] Based on several studies, mint leaves were shown to have high antioxidant content, antimicrobial, antitumor, and antialergenic.[12]

Acute toxicity tests were conducted to examine toxic effects occurring within a short time after administration of a substance. Generally, acute toxicity tests were carried out within at least 24 hours.[13] Determination of the lethal or toxic dose range was expressed as LD_{50}.[14] When a suspension did not cause mortality up to 14 days post-treatment, then the suspension could be categorized as a practically non-toxic suspension.[15] The LD_{50} value calculated by the probit analysis method was obtained as 1.92 g/kg BW. Furthermore, those in the range of 0.5 to 5 g/kgBW were categorized as moderate toxicity.[16]

Parameters of mortality that could be observed in mice administered with dosages of 1.5 g/kg BW and 2.0 g/kgBW were suspected of causing damage to the cerebellum in mice. The content of menthone and menthofuran in mice was proven to cause an increase in liver weight, hepatotoxicity, and damage to the cerebellum in a short time.[7] This damage was reinforced by clinical symptoms displayed in mice, such as the presence of incoordination, symptoms of depression, and decreased locomotor activity. In this study, the cerebellum was the part of the brain that controlled balance, orientation, body positioning, muscle tone, and coordination.[17] This was consistent with the findings of clinical symptoms in mice administered with dosages of 1.5 g/kgBW and 2.0 g/kgBW, including depression, lethargies, and decreased locomotor activity. However, an increase in liver weight was not observed. This was likely because a higher dosage could be required for such an effect to occur.

Observations of clinical symptoms on acute toxicity test of peppermint suspension indicated abnormalities in clinical symptoms at doses of 1.5 g/kgBW and 2.0 g/kgBW. Clinical symptoms that appeared were depression, standing hair, lethargies, and decreased locomotor activity. According to previous studies, peppermint was known to contain components such as menthol (45.34%), menthon (16.04%), menthofuran (8.91%), cis-carane (8.70%), 1,8-cineole (9.45%), neo-menthol (4.24%), and limonene (2.22%). Furthermore, the content of menthol isomers in mint (L-menthol, D-menthol, and D/L-menthol) in excessive administration could irritate the eyes, skin, respiratory system, and coordination system.[7] This could also result in contributing to the clinical symptoms that occurred during the study, besides the suspected cerebellum damage caused by methon and methofurane.

Toxicity could affect physiological response through several mechanisms, with effects ranging from mild to severe, depending on factors such as dose, exposure duration, and specific substances involved. Several pathways contributed to these effects, including the disruption of cellular homeostasis, slowly leading to the decline of physiological parameters like temperature, heart rate, and respiratory rate.[18] Toxicity could also trigger an inflammatory response by activating immune cells,[19] potentially leading to increased body temperature. Furthermore, when the toxic substance induced neurotoxicity, it could alter neurotransmitter levels, damage neurons, or interfere with ion channels,[20] causing abnormality in heart and respiratory rate. In this study, the physiological response parameters of the mice, such as heart rate, respiratory rate, and temperature, showed no abnormalities. The heart rate of the mice was in the range of 86 to 216 ×/min, which was still in the normal range, showing 85 to 216 ×/minute.[21] Respiratory rate observed after administration was in the range of 82 to 147 ×/minute, which was still in the normal respiratory rate of mice, indicating 80 to 230 ×/minute.[22] The temperature of the mice was in the range of 36.3 to 38.5°C, which was below the normal range, ranging from 36.5 to 38.0°C.[21] The temperature difference was influenced by room temperature and differences in the metabolic rate of the mice's body.

The body weight parameters of the mice did not show any significant increase or decrease, and there was no difference between the body weight of the control and the mice given peppermint suspension at several dosages. Subsequently, the body weight of mice in the treatment group was still within the normal weight range, which was 18 to 35 grams.[23]

Calculation of absolute weights and macroscopic observations of mice organs were conducted as an indicator of the presence or absence of toxic effects of a compound on the organs of experimental animals. Based on the recommendations of The Society of Toxicology

Pathology (STP), the organs that were used as indicators of acute toxicity tests were the liver, kidneys, spleen, lungs, and heart.[24] This was due to the close ties between these organs in the metabolic and detoxification processes. Macroscopic observations were made to observe whether there was damage to the organs. Damage observed such as changes in liver color to yellow-brown, cell degeneration, and the discovery of masses that indicated inflammation, either chronic or acute inflammation, abscesses, and malignant tumors.[25] Based on Figure 2, the administration of peppermint suspension did not result in any macroscopic changes in these organs or any differences in organ weights between control mice and mice given peppermint suspension administration in various doses. This proved that the administration of mint suspension did not influence any of the observed organs.

Absolute organ weight was one of the parameters that provided accurate results in toxicity testing of a substance to target organs, however, absolute weight measurement was often followed by relative organ weight measurement as the correlation was strong. Relative weight referred to the ratio between organ weight and animal body weight.[26] As a sensitive indicator of organ damage, changes in organ weight were difficult to interpret.[27] This could be caused by organ weight being affected by body weight, causing variation due to differences in body weight. Relative organ weights were analyzed for the same organs, namely the liver, innards, kidneys, lungs, heart, and spleen, which did not indicate any significant differences.

Based on the findings on the parameters, administration of peppermint suspension caused mortalities on the dosage of 1.5 g/kgBW and 2 g/kgBW. Mice administered with the dosage of 1.5 g/kgBW and 2 g/kgBW also revealed clinical signs such as depression, lethargy, standing hair, and decreased locomotor activity. However, no macroscopic lesions were shown on the organs observed, which were liver, innards, kidneys, lungs, heart, and spleen. No significant difference was displayed in physiological responses, body weight, and absolute and relative organ weight. According to the number of mortalities, the LD_{50} value of this study was found at 1.92 g/kgBW. Despite no macroscopic lesions shown, and no significant difference on any other parameter, the LD_{50} value showed that peppermint suspension administration in mice was in the moderate toxicity category. Based on the Hodge and Sterner test of toxicity (BPOM 2014)[15], the LD_{50} value of the moderate toxicity category was 0.5 to 5 g/kgBW. Compared to another study conducted by Malek et al.[7] the administration of peppermint oil towards mice proved that peppermint oil also fell into the category of moderately toxic (≤2 g/kgBW) towards mice, with an LD_{50} value of 1.6 g/kg BW. In another study conducted by Yousuf et al.,[8] acute toxicity of Japanese mint oil on brine shrimp indicated an LD_{50} value of 2070.4 µl/kg and was in the moderate category.

According to these findings, peppermint suspension administration on mice was in the category of moderate toxicity based on the number of mortalities and the clinical signs shown by the group administrated with a dosage of 1.5 g/kgBW and 2 g/kgBW, with the LD_{50} value of 1.92 g/kgBW. This suggested that administration above 1.92 g/kgBW of peppermint suspension could cause death or clinical symptoms such as depression, lethargy, and decreased locomotor activity. Furthermore, this study did not include microscopic observation of the organs, which could show any significant lesion that occurred microscopically toward the organs. Further studies must be carried out including microscopic observation of the organs, such as histopathology, to determine whether the suspension could affect organs microscopically.

References

1. Jumiarni WO, Komalasari O. Eksplorasi jenis dan pemanfaatan tumbuhan obat pada masyarakat suku wuna di pemukiman kota wuna. Traditional Medicine Journal. 2017;22(1):45–56.
2. Puspitasari L, Mareta S, Thalib A. Karakterisasi senyawa kimia daun mint (mentha sp.) dengan metode FTIR dan kemometrik. Sainstech Farma. 2021;14(1):5–11.
3. Chakraborty K, Chakravarti AR, Bhattacharjee S. Bioactive components of peppermint (Mentha piperita L.), their pharmacological and ameliorative potential and ethnomedicinal benefits: A review. J Pharmacogn Phytochem 2022;11(1):109–14. doi: 10.22271/phyto.2022.v11.i1b.14322.
4. Taherpour A, Khaef S, Yari A, Nikeafshar S, Fathi M, Ghambari S. Chemical composition analysis of the essential oil of Mentha piperita L. from Kermanshah, Iran by hydrodistillation and HS/SPME methods. J Anal Sci Technol. 2017;8(11):1–6. doi: 10.1186/s40543-017-0122-0

5. Jafarimanesh H, Akbari M, Hoseinian R, Zarei M, Harorani M. The effect of peppermint (Mentha piperita) extract on the severity of nausea, vomiting, and anorexia in patients with breast cancer undergoing chemotherapy; a randomized controlled trial. Integr Cancer Ther. 2020;19:1534735420967084. doi:10.1177/1534735420967084.
6. Kumar A, Baitha U, Aggarwal P, Jamshed N. A fatal case of menthol poisoning. Int J Appl Basic Med Res. 2016;6(2):137–9. doi: 10.4103/2229-516X.179015.
7. Malekmohammad, Khojasteh, Rafieian-Kopaei, Mahmoud, Sardari, Samira S, Robert. Toxicological effects of Mentha x piperita (Peppermint): a review. Toxin Reviews. 2021;40(4):445–9. doi: 10.1080/15569543.2019.1647545
8. Yousuf T, Akter R, Ahmed J, Mazumdar S, Talukder D, Nandi NC, et al. Evaluation of acute oral toxicity, cytotoxicity, antidepressant, and antioxidant activities of Japanese mint (*Mentha arvensis* L.) oil. Phytomedicine Plus. 2021;1(4):1–7. doi: 10.1016/j.phyplu.2021.100140
9. Hasibuan AL, Dalimunthe GI. Formulasi dan evaluasi sediaan patch transdermal yang mengandung ekstrak daun mint (Mentha piperita L.) sebagai antidiare. Journal of Health and Medicinal Science. 2022;1(4):100–8.
10. Sucianti A, Yusa NM, Sugitha IM. Pengaruh suhu pengeringan terhadap aktivitas antioksidan dan karakteristik teh celup herbal daun mint (Mentha piperita L.). Jurnal Ilmu dan Teknologi Pangan. 2021;10(3):378–88.
11. Sulastra CS, Khaerati K, Ihwan. Toksisitas akut dan lethal dose (LD50) ekstrak etanol uwi banggai ungu (Dioscorea alata L.) pada tikus putih (Rattus novergicus). Jurnal Ilmiah Medicamento. 2020;6(1):10–14.
12. Bourhia M, Lahmadi A, Achtak H, Touis A, Elbrahmi J, Ullah R, et al. Phytochemical analysis and toxicity study of aristolochia paucinervis rhizomes decoction used in Moroccan alternative medicine: Histopathological and biochemical profiles. Evidence-Based Complementary and Alternative Medicine. 2019;1398404. doi:10.1155/2019/1398404
13. Jaishankar M, Tseten T, Anbalagan N, Mathew BB, Beeregowda KN. Toxicity, mechanism and health effects of some heavy metals. Interdiscip Toxicol. 2014;7(2):60–72. doi:10.2478/intox-2014-0009
14. Garcia A, Santa-Helena E, de Falco A, de Paula Ribero J, Gioda A, Gioda CG. Toxicological effects of fine particulate matter ($PM_{2.5}$): health risks and associated systemic injuries –systematic review. Water Air Soil Pollut. 2023;234(6):346. doi:10.1007/s11270-023-06278-9
15. Liu J, Schelar E. Pesticide exposure and child neurodevelopment. Workplace Health Saf. 2014;60(5):235–43. doi: 10.1177/216507991206000507
16. Soltysinska E, Speerschneider T, Winther SV, Thomsen MB. Sinoatrial node dysfunction induces cardiac arrhythmias in diabetic mice. Cardiovascular Diabetology. 2014;13(1):1–11. doi: 10.1186/s12933-014-0122-y.
17. Ribeiro FM, Correia PMM, Santos AC, Veloso JFCA. A guideline proposal for mice preparation and care in F-FDG PET imaging. EJNMMI Research. 2022;12:49. doi:10.1186/s13550-022-00921-y
18. Guo X, Weng L, Yi L, Geng D. Toxicological safety evaluation in acute and 21-day studies of ethanol extract from Solanum Iyratum thunb. Evidence-Based Complementary and Alternative Medicine. 2022;15(5):392–400.
19. Perdana RM, Amir MN, Mamada SS. Pengaruh pemberian ekstrak etanol kayu secang (Caesalpinia sappan L.) secara subkronik terhadap bobot jantung dan paru tikus putih jantan (Rattus novergicus). Majalah Farmasi dan Farmakologi. 2020;24(2):63–6. doi: 10.20956/mff.v24i2.10683
20. Lazic SE, Semenova SE, Williams DP. Determining organ weight toxicity with Bayesian casual models: improving on the analysis of relative organ weight. Scientific Reports. 2020;10(1):1–12. doi:10.1038/s41598-020-63465-y