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Potential Impact Microplastic Polyethylene Terephthalate on Mice

Marchel Putra Garfansa[1], Roy Hendroko Setyobudi[2], Iswahyudi Iswahyudi[1], Shazma Anwar[3], Damat Damat[2], Tony Liwang[4], Mardiana Sri Susanti[5], Diah Hermayanti[2*], Meddy Setiawan[2], Thontowi Djauhari Nur Subchi[2], Dewi Mariyam[6], Yolla Muvika Ananda[2], Satriyo Krido Wahono[7], Adil Basir[8], Musrif Musrif[9] and Anwar Saeed Khan[10]

[1]Universitas Islam Madura, Pamekasan 69317, East Java, Indonesia; [2]University of Muhammadiyah Malang, Malang 65144, East Java, Indonesia; [3]University of Agriculture, Peshawar 25130, Khyber Pakhtunkhwa, Pakistan; [4]Plant Production and Biotechnology Division, PT Smart Tbk., Bogor 16810, West Java, Indonesia; [5]Aura Statistics Consultant, Malang 65141, East Java, Indonesia; [6]Center Research and Diagnostic "Satwa Sehat" Indonesia, Malang 65146, East Java, Indonesia [7]Research Center for Food Technology and Processing (PRTPP), National Research and Innovation Agency (BRIN) Special Region of Yogyakarta 55281, Indonesia; [8]University of Muhammadiyah Palopo, Palopo 91922, South Sulawesi, Indonesia; [9]Dayanu Ikhsanuddin University, Baubau, Buton, Southeast Sulawesi, Indonesia; [10]University of Peshawar, 25120 Peshawar, Khyber Pakhtunkhwa, Pakistan.

Abstract | Microplastic (MPs) pollution is an increasing global problem, creating deep concerns regarding its potential impact on human health. Numerous experiments have been conducted on living organisms to investigate the dispersion patterns of MPs. Furthermore, the extent of distribution and research conducted on MPs about mice still needs to be improved. This study aimed to determine the impact of PET (polyethylene terephthalate) MPs on mice's weight, feces, and appetite. Four feed experiments, P0 (pellet BR1), P1 (potato from Pujon Farm), P2 (potato mixed 300 μg PET), and P3 (potato mixed 600 μg PET), were investigated in this research. PET MPs at a dose of 600 μg had the worst impact on mice compared to the others. There were changes in eating performance, body weight, and mice feces in treatment P1 due to the MPs contained in them. Another consequence is anticipated: A reduction in microbial diversity in the intestines of mice, resulting in a fall in both feces and body weight of the mice.

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***Correspondence** | Diah Hermayanti, Department of Pathology, Faculty of Medicine, University of Muhammadiyah Malang, The 2nd Campus, Jl. Bendungan Sutami No.188, Malang 65145, East Java, Indonesia; **Email:** diahhermayanti_umm@yahoo.com
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Introduction

Microplastic (MPs) pollution is an increasing global problem, creating deep concerns regarding its potential impact on human health (Cao *et al.*, 2024). MPs, small particles (< 5 mm) originating from the decomposition of plastic (Yuan *et al.*, 2022), are increasingly widespread in water and soil environments (Li *et al*., 2023), increasing the risk of human exposure (Lee *et al*., 2023). Previous research shows that MPs can enter the human body through various pathways (Domenech and Marcos, 2021; Zhu *et al*., 2023), including food consumption, drinking water and air (Mamun *et al*., 2023; Setyobudi *et al*., 2024a, b). Chemicals contained in MPs, such as polychlorinated biphenyls (PCBs) (Yeo *et al*., 2020), can cause serious health problems, including endocrine disruption and decreased reproductive health (Montano *et al*., 2022). The buildup of MPs in human organs, such as the intestines and lungs, is a significant concern due to the potential toxic effects on body tissues (Barceló *et al*., 2023). Moreover, the presence of MPs in everyday consumer products, such as food and drinks (Setyobudi *et al*., 2024a, b; Sewwandi *et al*., 2023), shows the urgency of the need for this research as a basis for developing consumer protection policies. In some cases, MPs have been linked to inflammatory diseases and cell damage (Xu *et al*., 2023), raising concerns about the risk of chronic disease. Ethical considerations also arise as the potential impact of MPs on human health requires careful assessment and regulation.

In the context of globalization and human mobility, analyzing the impact of MPs on human health has also become an urgent public health issue. Several studies have been carried out to examine the long-term effects of MPs on organisms, including mammals. In males, MPs can cause abnormal testicular and sperm structure, decreased sperm vitality, and endocrine disruption, leading to reproductive system damage (Angelo and Meccariello, 2021). In females, MPs can result in abnormal ovary and uterus structure, endocrine disruption, and tissue fibrosis (Afreen *et al*., 2023). Microplastics exert a profound impact on wildlife, particularly marine species. Marine animals, including fish, seabirds, and mammals, frequently mistake microplastics for food (Prata *et al*., 2022). Upon ingestion, these particles can inflict physical harm on internal organs, leading to injuries or obstructions within the digestive system. Moreover, microplastics often carry or adsorb toxic chemicals, which can leach into the bodies of these animals, disrupting endocrine systems and impairing reproductive functions (Liu *et al*., 2023).

Previous studies have shown that maternal exposure to MPs can lead to premature mortality in offspring, as well as metabolic disorders, reproductive dysfunction, immune, neurodevelopmental, and cognitive disorders (Hong *et al*., 2023). MPs have been found to alter the physiology and behavior of marine invertebrates and fish (Park and Kim, 2022), and mice models have shown impacts on blood parameters, erythrocyte deformation, and liver and kidney functions (Deng *et al*., 2017). The effects of MPs on mammalian cells and organisms are still being explored. Still, studies have indicated oxidative stress, apoptosis, inflammatory response, dysregulation of the endocrine system, and accumulation in various organs as possible consequences (Ali *et al*., 2024).

Additionally, there is a concern about the accumulation of MPs in human and animal tissues, potentially negatively affecting reproductive physiological functions (Dubey *et al*., 2022; Xie *et al*., 2020). Numerous experiments have been conducted on living organisms to investigate the dispersion patterns of MPs. Furthermore, the extent of distribution and research conducted on MPs about mice still needs to be improved, surprising findings regarding the impact of MPs on mammals. Mice exposed to MPs showed significant reductions in reproductive health (Hou *et al*., 2021). Moreover, Jin *et al*. (2021) discovered that mice exposed to PS-MPs measuring 4 μm and 10 μm saw reduced feed consumption and body weight. However, no notable changes were detected in the group exposed to 0.5 μm PS-MPs. These findings raise critical questions regarding the impact of MPs on mammalian metabolism systems. The high mortality in mice exposed to MPs is also the research focus. Researchers found that MPs damaged mice's immune systems, increased their likelihood of developing infectious diseases (Sun *et al*., 2021), and led to earlier deaths. This underlines the urgency of further research regarding the immunological impact of MPs on mammals.

Additionally, the study noted structural and biochemical changes in the organs of mice exposed to MPs. MPs showed significant damage, raising concerns about the potential long-term effects on the function of mammalian organs. Polyethylene exposure impacted the liver and renal functioning (Abdel-Zaher *et al*., 2023), disturbed the detoxification response, promoted oxidative imbalance, and increased inflammatory foci and cytokine expression (Djouina *et al*., 2023). Meanwhile, polypropylene exposure did not cause obvious health symptoms.

Still, hematoxylin-eosin staining showed pathological changes that polypropylene-induced lipid droplet accumulation in the liver decreased the first polar body extrusion mice and the survival mice of super ovulated oocytes causing polystyrene in mice (Liu *et al*., 2022). Polyethylene terephthalate exposure has investigated that chronic and physiological low-dose exposure of PM-PET did not affect intestinal pathology and mucin barriers, respectively (Harusato *et al*., 2023).

Further investigation of mice metabolism is needed to understand the biological response to exposure to MPs and the potential long-term risks to mammalian health in PET. It is still unclear whether the effect of MPs on feces, weight, and appetite in the bodies of mice is caused by MPs. These findings provide a foundation for further research to fill the knowledge gaps in this field.

This study aims to determine the impact of PET MPs on the weight, feces, and appetite of mice. Given the effects of MPs on model organisms such as mice, this research is essential for understanding the physiological and pathological changes that humans may experience due to exposure to MPs. MPs can potentially affect human health (Emenike *et al*., 2023), primarily through imbalances in homeostasis and chronic inflammation (Zhao *et al*., 2024). By investigating the impact of MPs on mice in-depth, this research will provide a solid scientific basis for assessing similar risks in humans. The implications of human health issues in this context include potential immunological changes and systemic disorders that must be further understood to protect global public health. Therefore, this research is relevant for understanding MPs at the ecosystem level and essential for driving public health and environmental protection policies.

Materials and Methods

Experimental animal and housing condition

Eight-week-old male *Rattus norvegicus* (Berkenhout, 1769). Each mouse was placed in a glass cage (300 mm × 300 mm × 300 mm) with a wire floor during the study period. Under each cage, a plastic tray filled with sawdust was placed, covered with a sheet of paper. All mice were placed in Experimental Animal Cages, Pharmacology Laboratory, Faculty of Medicine, University of Muhammadiyah Malang, the 2nd campus (coordinates: S 7°57'27.1332" and E 112°36'50.7312") at constant temperature (28 °C ± 2 °C), humidity (55 % ± 10 %), and an 8-hour light/16-hour dark cycle (lights on at 09:00 and off at 17:00). Mice were given feed according to treatment and given tap water (mixed with filtered water from a blender potato) ad libitum. The description of ethical approval carried out the experiment No. E.5a/211/KEPKUMM/VII/2023, issued by the Health Research Ethics Commission, Faculty of Medicine, University of Muhammadiyah Malang.

Feed preparation

Potato (*Solanum tuberosum* L.) as mice feed was purchased from a potato farm at Maron hamlet, Pujon Kidul village, Pujon subdistrict, Malang Regency (coordinate: S 7°51'20.0664" and E 112°28'18.4152"). Male mice were purchased from Mice Breeding Centre (coordinate: S 8°0'22.1508" and E 112°37'40.1592"). PET – MPs (used plastic bottles) were crushed using a blender until smooth and filtered using a 5 mm filter.

Experimental design

The feed formula was prepared as follows : P0 (pellet BR1), P1 (Potatoes Pujon Kidul farm), P2 (potatoes and 300 μg PET per day), and P3 (potatoes and 600 μg PET per day). The dose of 600 μg PET per day refers to previous research (Hermayanti *et al*., 2024; Li *et al*., 2023); this study used eight mice per treatment with a total of 32 mice. Feed consumption per mouse was 5 g in 1st wk and 20 g in 2nd wk until the research was finished. Potato feed in the 1st wk is given as thick porridge, namely potatoes blended and filtered. Filtered water is mixed with drinking water. In the 2nd wk, the feed is given in the form of thick porridge plus potatoes cut into 2 mm pieces, and in the 3rd wk it is given in the form of potatoes cut into 2 mm pieces. Mice will be adapted to feeding BR1 pellets for 7 d, before being given special treatment (P0 to P3).

The BR1 was a feed produced by PT Japfa Comfeed – Indonesia. Hermayanti *et al*. (2024) and Setyobudi *et al*. (2024a) reported that the gross energy (GE) in BR1 feed was .4 131.24 %, lower than potatoes from Pujon Farm, which was 4 359.75 %. They have also reported that potatoes at Pujon Farm were declared contaminated with MPs particle amounting to 0.05 g^{-1} and with Stanum (Sn). This MPs and Sn contamination is higher than samples from two other potato cultivation areas in Malang Raya (Setyobudi *et al*., 2024a).

Score observation

The status of mice was monitored in this study. Body weight, feed left, and feces were measured using an electronic scale (PE-1600, Mettler Ltd., Tokyo, Japan). Body weight and feed left were measured every week for 3 wk, while feces were measured at 1st wk, 2nd wk, and 3rd wk. Feed consumption per animal was determined by determining the known weight and weighing the amount of food remaining after 7 d. Water consumption is measured in the same way. Survival mice were assessed throughout the animal's lifetime. Deaths due to natural causes were recorded.

Statistical analysis

Data are expressed as means ± SD. Differences were tested using an analysis of variance (ANOVA) and a Tukey post hoc test. The data were tested statistically for normality using Shapiro–Wilk (S–W) tests and to test the homogeneity of variance using the Levene test. Then, the comparison test for body weight, feces weight, and fed left were analyzed using SPSS 18 (Adinurani 2016, 2022).

Results and Discussion

Effect of microplastic on weight

Feeding mice with microplastic contamination makes a real difference to the weight of the mice every week. Changes in the body weight of mice after being given food contaminated with microplastics are presented in Figure 1.

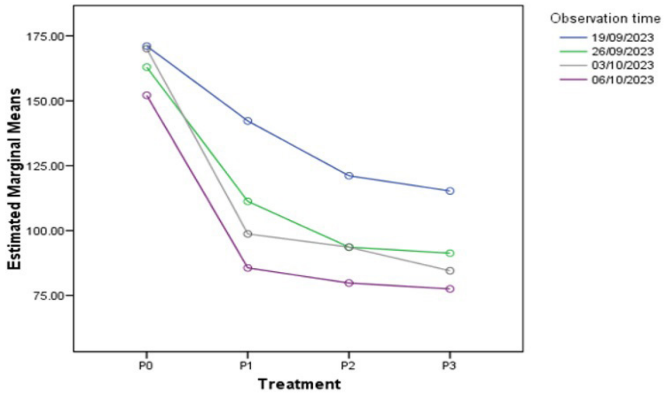

Figure 1: *Mice weight in different treatment.*

In general, feeding mice with microplastic contamination makes a real difference to the weight of the mice every week. Changes in the body weight of mice after being given food contaminated with microplastics. The data shows that administering a dose of microplastics to mice had a natural effect on the weight of the mice by reducing the weight of the mice. With increasing doses of microplastics given, the weight of the mice decreased. On 09/19/2023, treatment P0 had the highest mice weight of 171.125 g, followed by P1 with 142.25 g, P2 with 121.125 g, and P3 with 115.250 g. At this date, P0 was the heaviest treatment, while P3 was the lowest treatment. P0 was a control treatment that ensured no microplastic content in this study. There was a decrease of 16 % when P1 was given compared to the control. In the first observation, the reduction in mice weight further increased to 29 % and 32 % when the mice were given microplastic doses of 300 μg and 600 μg, respectively. A similar thing was seen on the observation dates 09/26/2023, 10/03/2023, and 10/06/2023; P0 showed the highest mice weight, followed by P1, P2, and P3. Long-term exposure to MPs resulted in a significant reduction in the weight of mice. The weight loss of mice continues to occur due to feeding them food contaminated with microplastics. The weight of mice in the P0 treatment also decreased at each observation time, although not as drastically as other observations. This decrease was caused by stress in the mice during the experiment period. During observations on 09/26/2023, the mice's weight was decreased for all treatments with weights of 163.000 g, 111.250 g, 93.625 g and 91.286 g in treatments P0, P1, P2 and P3, respectively.

Furthermore, at the last observation (06/10/2023), there was also a significant decrease ($P > 0.05$). There was a decrease in mice weight by 43 %, 47 %, and 49 % compared to treatment P0 with treatment P1, P2, and P3, respectively. Weight loss was higher in the last observation, with the potential for weight loss being 49 % compared to the P3 treatment. However, treating P1 (local potato product) also resulted in significant weight loss. Sufficient weight loss will hurt mice by injuring several internal organs and causing death. Figure 2 reveals a relationship between weight loss and the number of mice deaths in this study. Mice death was observed at the end of the observation by dividing the number of live mice by the number of dead mice. Data shows that mortality occurred at 6.3 %, 12.5 %, 18.8 %, and 34.4 % in treatments P0, P1, P2, and P3, respectively. The potential for mice death was highest in the P3 treatment and almost reached six times compared to the P0 treatment. The P1 treatment also showed quite high mortality compared to P0; likewise, when the addition of 300 μg was added, 18.8 % mortality occurred.

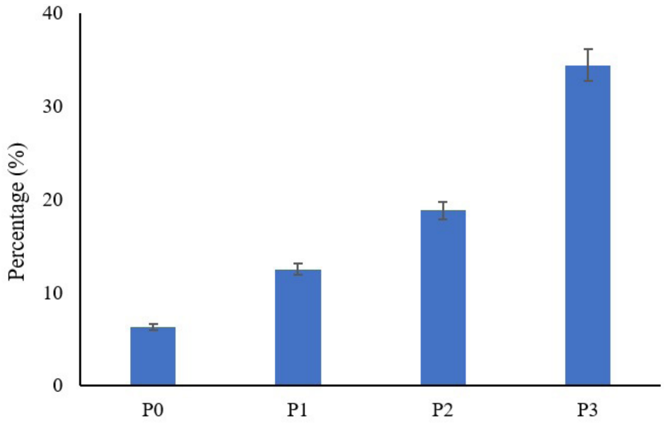

Figure 2: *Death mice in different treatment.*

Effect of microplastic in feces

Feces weight was measured to determine health parameters in mice. Some of the effects of the treatment given to mice are shown in Figure 3. The first observation (26/09/2023) showed no significant change between treatment P0 and P1 in the weight of mice, as well as P2 and P3. However, the reduction in feces weight was relatively high in treatments P2 and P3 compared with P0.

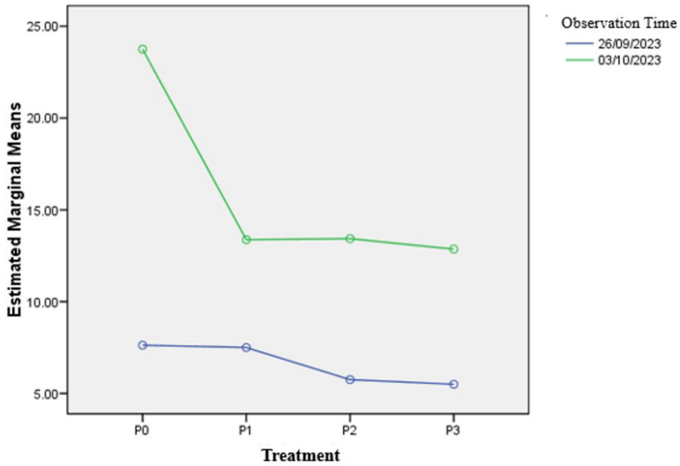

Figure 3: *Feces weight in different treatment.*

There was a decrease in feces weight of 24 % and 27 % in treatments P2 and P3, respectively, when compared with P0. Treatment P3 showed the lowest mice feces, 5.5 g, while P1 and P0 had the heaviest feces, 7.5 g and 7.625 g, respectively. Treatment P2 included 5.75 g of feces. Differences in feces weight between treatments can be caused by variations in the digestive system of mice given food with different compositions. The P3 treatment, which had the lightest feces, may reflect the adverse effects of exposure to 600 μg MPs on rat digestion, resulting in less residue. In the second observation (03/10/2023), the weight of the feces decreased sharply, reflecting the strong influence of microplastics on the weight of the feces produced. The decrease in feces weight was 43 % in treatment P1 compared to P0. Adding 300 μg (P2) and 600 μg (P3) also reduced the weight of mice by 43 % and 45 % compared to P0. This proves that adding microplastics can reduce the weight of rat droppings, and it is likely that the weight will continue to decrease if additional microplastics are carried out. In treatments P1, P2, and P3, the feces weight tended to be flat, indicating that the potential damage caused to mice was the same or not significantly different. So, it can be concluded that P1 has the potential to inhibit the same danger as treatments P2 and P3 because P1 was contaminated with MPs particles and Stanum (Sn).

Effect of microplastic in feed leftover

Feed left was significantly influenced by microplastic dose at each observation. In the results of the interaction between group (P0, P1, P2, and P3) and observation time (1st wk, 2nd wk, and 3rd wk), a sig value was obtained to 0.049 ($P < 0.05$), so it can be concluded that there is a significant difference in feed leftover (g) between the interactions between groups (P0, P1, P2, and P3) and observation time (1st wk, 2nd wk, and 3rd wk) presented in Figure 4.

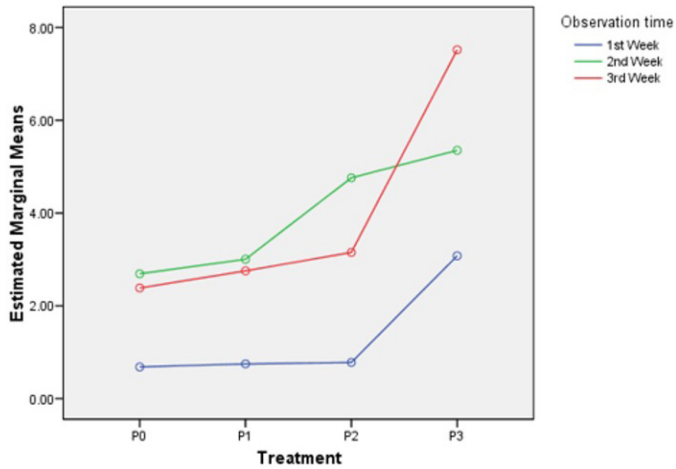

Figure 4: *Feed leftover in different treatments.*

In experiments observing treatments at various times, comparing feed left over between treatments can provide an exciting picture. In the 1st wk, treatment P0 showed the lowest feed leftover at 0.684, while treatment P3 had the highest feed left over reaching 3.079. The P0 treatment may have shown the lowest feed leftover due to an early response to the unfamiliarity of the potatoes provided. In the 1st wk, feed leftover P0, P1, and P2 showed a flat pattern and in treatment P3, feed left- over increased in height by 3 g. The same thing was also demonstrated by P3 treatment in the 2nd wk and 3rd wk of observation. The reduced appetite of mice was proven to be due to the influence of the dose of MPs, the highest peak of feed left over was shown in the 3rd wk of observation of P3 treatment. There is a 68 % difference in feed leftover in P3 compared to P0. For both 1st wk and 3rd wk of observation, P0 still showed the lowest feed left over compared to other treatments. Feed leftover began to increase when the dose of MPs was added to the mice feed samples. In the 2nd wk there was a difference of 69 % (P2) and 98 % (P3) when compared with P0. This increase is also relevant to prove the influence of microplastics on feed leftover by mice. In the 3rd wk of observation, treatments P0, P1, and P2 showed lower feed leftover values than in the 2nd wk of observation. This may be due to increased mice appetite in the 3rd wk. However, in treatment P3, the residual value feed abandonment increased sharply beyond 2nd wk.

Impact of PET - MPs on animals

MPs, especially PET, pose a severe threat to animal life. The impact of PET - MPs on various types of animals and the potential consequences are presented in Figure 4. PET - MPs can pollute animal life (Prata *et al.*, 2022). Consumption of MPs by animals can cause poisoning and accumulation in the food chain (Collin-Faure *et al.*, 2023), and can potentially cause health problems (Singh and Mishra, 2023) and reproduction. Studies show PET MPs accumulating in the digestive system can cause structural disorders and mammalian biochemistry (Liu *et al.*, 2023). The impacts include organ dysfunction and behavioral changes in these animals. Pets such as dogs and cats are also susceptible to the effects of PET - MPs (Zhang *et al.*, 2019). Research shows that MPs can cause digestive disorders, hormonal dysfunction, and other health problems in pets (Yin *et al.*, 2021).

When discussing the possible impacts of exposure to PET - MPs, it must be acknowledged that the negative consequences are influenced by the size and number of MPs (Osman *et al.*, 2023). Smaller particles can penetrate tissue, causing cell damage (Tabel 1) (Ghosh *et al.*, 2023). As a follow-up, awareness of the impact of MPs on various types of animals is crucial (Zhao *et al.*, 2024). Proactive measures, such as reducing the use and waste of MPs, are needed to protect animal lives from this serious risk.

Contaminated feed poses a substantial threat to the health of mice, leading to critical issues such as weight loss, reduced appetite, and digestive disorders. Specific contaminants, notably MPs, exhibit pronounced toxic effects. In this study, differences in mice weight between treatments may be caused by variations in feed composition causing MPs. Furthermore, P0 has a higher nutritional protein content, which explains the mice's highest weight. Mice fed a low-protein diet had lower body weight than those on an adequate-protein diet (Chaumontet *et al.*, 2018). Another study found that different feeding diets, such as lipid (Wang*et al.*, 2022), carbohydrate, and protein (Kondo *et al.*, 2023), had varying effects on blood biochemical profiles in mice, including glucose, cholesterol, and total protein levels (Lewicki *et al.*, 2018). Maternal undernutrition also negatively affects offspring body composition (Wu *et al.*, 2022). Pelleted food for animals offers

Table 1: *Experimental research on the effect of MPs on animal.*

Animal	Polymer type	Dose	Size	Impact	Reference
Micetus norvegicus	PET	(300 to 600) mg d^{-1}	5 µm	Reducing the weight of feces, appetite, body weight	Present study
Micetus norvegicus	PET	-	100 µm to 200 µm	Impact on the transcriptome in gut immune cells and their metabolisms	Harusato *et al.*, 2023
Apostichopus japonicas	PET	103 to 105, particle kg^{-1}	0.5 µm to 200 µm	The amylase and trypsin activities showed significant indigenous changes and a dose-dependent effect	Zhang *et al.*, 2023
Drosophila	PET	1 g L^{-1}	-	Decrease of triglyceride and glucose content in male flies	Liang *et al.*, 2022
Mytilus galloprovincialis	PET	(0.0005 to 100) mg L^{-1}	100 µm	Decrease the sex hormones estradiol and testosterone in mussels	Choi *et al.*, 2022
Caretta caretta	PET	0.03 g to 0.11 g	1 µm	Gastrointestinal impairment	Di Renzo *et al.*, 2021

several nutritional benefits. Pelleting improves the digestibility of nutrients and energy in pigs, leading to increased feed efficiency and growth performance (Lancheros *et al*., 2020). It also increases dry matter intake and average daily gain in small ruminants, improving their production performance (Retnani *et al*., 2022). Variability in mice weight in various treatments and observation times can be explained by complex factors that influence biological responses (Navarro *et al*., 2021).

Meanwhile, P2 and P3 had a negative influence on the weight of mice, explaining the significant decrease in mice weight. Ilechukwu *et al*. (2022) showed a mice's body weight reduction due to exposure to 10 g polystyrene kg^{-1}feed. A significant decrease in the body weight of mice after 6 wk of exposure to polystyrene MPs has been reported too by (Xie *et al*., 2020). The presence of modified potatoes impacted the weight loss of mice in treatment P1 compared to P0. The GE in P0 (BR1) feed was 131.24 %, but in P1 (potatoes from Pujon Farm) it was 359.75 %. P1 exhibited the most significant drop in mice weight compared to P0 (P< 0.05). This demonstrates that using MPs in food processing significantly reduces the weight of mice. P1 was involved in conventional potato growing in Pujon, Indonesia. Agricultural land significantly contributes to microplastics in food products, which can cause various harmful effects when consumed (Cusworth *et al*., 2024). This study demonstrates that MPs in P1 inhibit metabolism and oxidation in mice. MPs disrupt metabolic pathways, including arachidonic acid metabolism (Zhang *et al*., 2023), causing harm to organs such as the hepatopancreas in shrimp and the liver, kidney, and spleen in chickens (Meng *et al*., 2022). Similar reductions also observed in this research may be due to the difficulty in expelling larger-sized MPs from the body, resulting in a heavy burden on the gastrointestinal tract, which may reduce feed absorption and cause decreased body weight (Jin *et al*., 2021).

Male mice exposed to polystyrene MPs for 21 wk showed a significant decrease in testicle relative weight (Ijaz *et al*., 2021). Similarly, repeated oral administration of polyethylene MPs in mice resulted in inflammation in the lung tissue, indicating toxicity and potential weight loss (Lee *et al*., 2022). Reducing weight in mice can potentially increase mortality, with the lowest death percentage in treatment P0 (6.3 %) and increasing to 12. 5%, 18.8 %, and 34.4 % in treatments P1, P2, and P3, respectively (Figure 2). The percentage of mice deaths was higher every time the microplastic dose was added. This increase in the percentage of deaths occurred due to a significant reduction in the body weight of the mice due to the high dose of microplastics, which caused problems in the mice. Weight loss in mice is associated with disrupted sleep/wake patterns and altered gene expression (Hou *et al*., 2019).

Moreover, gradual weight loss and hypothermia were observed as signs of imminent death in mice (de Evsikova and Evsikov, 2023; Wiedmer *et al*., 2021). Furthermore, (Park *et al*., 2020) observed that Crucian carp [*Carassius carassius* (Linnaeus, 1758)] exposed to medium and high concentrations of MPs experienced a decrease in weight compared to the control group. This variability shows that the mice's weight response to treatment varied at each observation time, with some treatments showing quite large fluctuations between observations. Doses of MPs can lead to weight loss in mammals, including mice (Prata *et al*., 2022).

MPs can lead to intestinal disturbances such as gut microbe. Moreover, the gut microbiota is pivotal in digestion and absorption, synthesis of vitamins, immunological response, and maintenance of the gut barrier. Furthermore, it strongly correlates with the host's overall health. When micro and nanoplastics enter the intestines, they interact with the gut microbiota, potentially impacting its composition and function (Jin *et al*., 2019). Moreover, ingestion of MPs can also cause liver toxicity, inflammation, and lipid accumulation in mammals, as well as oxidative stress (Liang *et al*., 2024). These disruptions in the digestive system can have negative impacts on the health and development of animals, including growth inhibition and restricted development of embryos (Wang *et al*., 2022b).

On the other hand, P1 and P0 with higher feces in mice may indicate that the type of feed, such as farmer's potatoes and pelleted feed, has a more significant impact on feces formation. The decrease in feces weight was also caused by the low amount of feed consumed by mice. It is shown in Figure 4 that high doses of MPs increase feed leftover given to mice. It is essential to understand the influence of a poor appetite on digestion and stool weight in the context of gastrointestinal health. Based on recent research, there is a significant relationship between these aspects. Consuming minimal feed can harm digestion by reducing fiber intake and essential nutrients. As a result, the digestive process becomes slow, and the activity of digestive enzymes can be disrupted, resulting in looser stools.

On 03/10/2023, the comparison pattern changed. Treatment P0 had the highest feces in mice, reaching 23.75 g, higher than other treatments. The decrease in feces by mice occurred in P1, although not so drastic. The low MPs content in treatment P1 begins to affect the mice's feces and can affect the microbiota in the mice's intestines (Zingaro *et al*., 2023). Polyethylene MPs can cause significant changes in the gut microbiota of mice (Li *et al*., 2020). At the phylum level, Firmicutes in the feces of the MP group decreased, while Bacteroides increased significantly (Sun *et al*., 2021). These changes may affect digestive function and the balance of gut microbiota, contributing to changes in feces mice and digestive health. Treatments P2 and P3 had almost the same mice feces, with P2 slightly higher (13.429 g) than P3 (13.375 g). Treatments P2 and P3, which have nearly the same dirt as mice, can be caused by the dose of MPs given, although P3 slightly increases. The consistency of P3 as a treatment with the lowest feces in mice can be attributed to the higher dose and possible long-term effects of MPs. In this context, the effects of MPs on the digestive system of mice need to be further understood, and the observed fluctuations may be related to the complexity of the interactions between food type, MPs dose, and the physiological response of mice. These results indicate that treatment effects may vary depending on the observation time, with significant fluctuations in some treatments.

Mice exhibited signs of anxiety and took longer to eat in a new environment compared to their home cage (Francois *et al*., 2022). However, the social context influenced the response to unfamiliar feed (Siddiqui *et al*.,2022). Direct encounters between unfamiliar female mice did not result in significant social transmission of food preference (STFP), regardless of offensive agonistic behavior (de Vallière *et al*., 2022). On the other hand, an unfamiliar female's olfactory marks effectively promoted STFP. The response to a novel object in a familiar environment was avoidance and burying, while in a novel environment, mice increased their contact with the object and reduced burying. Rearing conditions also influenced these responses, with mice reared in an enriched environment exhibiting more contact with novel objects (Horii-Hayashi *et al*., 2021). In contrast, P0 and P1, who received pelleted feed or farmer's potatoes, may have adapted more quickly, explaining the high levels of feed left over in the 1st wk. In the 2nd wk, P3 maintained the lowest feed leftover with a value of 2.693, while P1 was the treatment with the highest feed leftover, reaching 4.760. P3 still had the lowest feed leftover, possibly due to the negative impact of the 600 µg MPs dose. P1 with farmer's potatoes could have high feed left over due to the mice's adaptation to this type of feed. The shift to the 3rd wk, with P3 having the highest feed leftover, may reflect the accumulation of toxic effects of MPs. However, a change occurred in the 3rd wk, where P3 now had the highest feed leftover at 2.385, and P0 still became the treatment with the lowest feed leftover reaching 7.520. Treatment P3 showed a consistent increase in feed leftover, possibly because the 300 mg MPs dose provided a milder stimulus, causing adaptation and increased appetite. In contrast, P0 had the highest feed leftover in the 1st wk but decreased in the following weeks. Changes in value are a form of the behavior pattern of mice towards the food they are given. Mice may experience aversion to feeding contaminated with MPs due to undesirable changes in taste or aroma (Gaspar *et al*., 2023). Moreover, a compromised immune response can affect mice's eating behavior and cause them to leave less food (Bhuyan, 2022). These results emphasize the complexity of the interactions between feed type, MPs dose, and experiment duration. These results indicate that the effects of treatment on feed leftover may vary depending on the time of observation, highlighting the complexity of the interactions between treatment factors and experimental duration.

Conclusions and Recommendations

This research tested the impact of PET- MPs doses on mice through direct feed intake. The effect caused by PET - MPs can reduce the body weight, weight of feces, and appetite of mice. PET-MPs at a dose of 600 µg had the worst impact on mice compared to the others. There were changes in eating performance, body weight, and mice feces in treatment P1 due to the MPs contained in them. Another consequence is anticipated: A reduction in microbial diversity in the intestines of mice, resulting in a fall in both feces weight and body weight of the mice. The influx of MPs into their digestive tract can diminish the mice's appetite. Nevertheless, the authors' findings are tentative and require additional investigation.

Further investigation is warranted to examine the levels of serum glutamic oxaloacetic transaminase (SGOT) or aspartate aminotransferase (AST), as well as serum glutamic pyruvic transaminase (SGPT) or alanine aminotransferase (ALT). Additionally, the authors have scheduled a liver histopathology study and the quantification of antibody expressions using immunohistochemistry (IHC) in *Rattus norvegicus*.

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Novelty Statement

The author has reviewed Google Scholar with publication times in the last ten years. However, the author has yet to find similar research, namely *in vivo* research on *Rattus norvegicus*, fed potatoes contaminated with PET-MPs. With these facts, the author states the novelty of this research, considering (i) potatoes are a staple food in several countries in the world, (ii) PET is a plastic polymer that producers and the public widely use, and (iii) the dangers of PET-MPs on the health of *Rattus norvegicus* which, as reported in this study, is a means of understanding the physiological and pathological changes that humans may experience due to exposure to PET-MPs.

Author's Contribution

Marchel Putra Garfansa: Writing original draft, conceptualization, writing review and editing, and literature search.
Roy Hendroko Setyobudi: Conceptualization, methodology, validation, writing – review and editing, literature search, Turnitin, Grammarly Premium check, and guarantor.
Iswahyudi Iswahyudi and Shazma Anwar: Data collection and investigation.
Damat Damat and Tony Liwang: Research supervision and elaborate the intellectual content.
Mardiana Sri Susanti: Data acquisition, formal analysis, and visualization.
Diah Hermayanti: Project administration.
Thontowi Djauhari Nur Subchi: Funding acquisition.
Meddy Setiawan, Satriyo Krido Wahono, Adil Basir, Anwar Saeed Khan and Musrif Musrif: Performed literature search and manuscript review.
Dewi Mariyam and Yolla Muvika Ananda: *Rattus norvegicus* health analyses.
All authors have read and approved the final manuscript.

Conflict of interest
The authors have declared no conflict of interest.

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