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THE EFFECTS OF SUBCHRONIC CADMIUM EXPOSURE ON INSULIN AND RELATED BLOOD BIOCHEMICAL INDICATORS IN MICE

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ABSTRACT

Background: Cadmium (Cd), as a common environmental pollutant, has been widely proved to be carcinogenic and toxic to multiple organs. However, the mechanism of low-dose and long-term exposure on pancreatic function is still unclear, especially its association with diabetes development needs to be verified by experiments. **Objective:** This study armed to explore the dose-dependent effects of subchronic cadmium exposure on insulin secretion, glucose metabolism and liver and kidney function in mice, and to provide experimental evidence for the toxic mechanism of cadmium-induced diabetes. Methods: 30 ICR mice were randomly divided into three groups, each group with 10 mice: control group (pure water), low dose group (50 mg/L $CdCl_2$) and high dose group (200 mg/L $CdCl_2$). The mice were poisoned by drinking cadmium solution and pure water for 14 weeks, and the body weight, blood routine, urine routine, fasting blood glucose/insulin and liver and kidney function indexes were detected. **Results:** Compared to the control group, the body weight of the cadmium-exposed mice did not change significantly after 14 weeks of exposure to cadmium. However, the high-dose group showed a decrease in white blood cells (down 12.3%), hemoglobin (down 9.8%), and hematocrit (down 7.5%) ($P < 0.05$). The urinary creatinine levels were significantly higher in the low-dose group (275.80±33.194 μmol/L) and the high-dose group (276.77±27.098 μmol/L) than in the blank control group (223.02±41.678 μmol/L), while the urinary β2-microglobulin levels were notably increased in the high-dose group (6.70±3.054 vs 11.985±6.046ng/mL). Fasting serum insulin levels were significantly lower in the low-dose group (249.76±5.827pg/mL) and the high-dose group (178.32±19.851pg/mL) than in the blank control group (290.24±23.919pg/mL), but there was no significant difference in blood glucose levels among the three groups. Fasting serum alanine aminotransferase and aspartate aminotransferase concentrations were higher in the low-dose and high-dose groups compared to the blank control group, with statistically significant differences ($P < 0.05$), while there were no significant differences in creatinine, urea, or urea/creatinine ratios ($P > 0.05$). **Conclusions:** Subchronic cadmium poisoning can inhibit insulin secretion in mice and cause partial liver and kidney damage, suggesting that cadmium pollution may increase the risk of diabetes through multi-organ interaction. This study provides a scientific basis for setting environmental cadmium exposure threshold and prevention and control strategies.

KEYWORDS: Cadmium, mice, insulin, toxicity, liver function.

1. INTRODUCTION

Metal cadmium (Cd) and its compounds classified as human carcinogens in 1993 by the International Agency for Research on Cancer and ranked seventh on the 2017 agency for Toxic Substances and Disease Registry.[1,2] In industry, cadmium is primarily used in mining, smelting, metallurgy, machinery, electroplating, manufacturing, soldering, pigments, batteries, and semiconductor components. In daily life, cadmium is mainly absorbed by the human body through the atmosphere, food, and water sources. Due to its long half-life, once absorbed by the human body, cadmium is difficult to metabolize, leading to damage to various tissues and organs. Studies have found that cadmium ions can indirectly induce the production of free radicals after entering cells, affecting a series of cellular signal transmissions and even causing cell apoptosis. Besides producing free radicals, cadmium can also participate in calcium ion metabolism processes in cells, thereby affecting the absorption and excretion of calcium. Additionally, cadmium can inhibit the activity of natural killer cells, reducing the body's immune function.[3] In summary, exposure to cadmium can cause multifaceted toxicity in the human body, leading to functional disorders in multiple organs or systems such

as the kidneys, heart, bones, respiratory system, endocrine system, and reproductive system. Long-term exposure to cadmium can also trigger related tumors.

Data shows that cadmium concentrations in the environment are high in many regions of our country. With the acceleration of industrialization, cadmium pollution in some areas will worsen.[4] Therefore, the prevention and control of cadmium pollution have become increasingly important. Currently, effective measures for preventing and controlling cadmium pollution mainly include physical isolation of contaminated soil, controlling excessive mining of zinc ore, and strictly monitoring the cadmium content in wastewater and exhaust gas according to emission standards. However, while these measures can control the occurrence of cadmium pollution to some extent, they also have significant negative impacts on the development of relevant industries.[5] In today's rapidly advancing biological sciences, using biological methods for effective detection and prevention of cadmium pollution is a new approach for future efforts in cadmium toxicity control.[6]

Research has found that the serum and urinary cadmium concentrations in diabetic patients are higher than those in normal individuals. Clinical observations and animal experiments have shown a close relationship between cadmium and impaired pancreatic function, insulin resistance, with its onset occurring much earlier than the time when cadmium causes cancer.[6,7] In recent years, research on the mechanisms of cadmium toxicity has attracted significant attention from scholars, while reports on the mechanism of cadmium-induced diabetes are scarce. Studies indicate that cadmium could damage human pancreatic cells, particularly causing β cell toxicity, leading to decreased insulin levels or exacerbating insulin resistance, thus resulting in elevated blood glucose levels. The increase in cadmium concentration in the human body is significantly associated with the development of type 2 diabetes.[8] Scholars have found a positive correlation between population cadmium load and the incidence of type 2 diabetes (T2DM). In terms of cadmium toxicity, for every 1 μg/g creatinine increase, the risk of T2DM increases by 16%. In occupational populations, insulin levels are inversely related to urinary and blood cadmium concentrations, indicating that occupational exposure to cadmium can alter insulin levels, leading to changes in blood glucose levels. Studies show that low-dose and long-term cadmium poisoning could lead to change in insulin levels in mice, subsequently causing disordered glucose and lipid metabolism. However, different study reports inconsistent results from animal experiments involving cadmium poisoning, especially in low-dose poisoning experiments, where some individual results even contradict each other. Therefore, it is essential to further explore and clarify the impact of cadmium on mouse pancreatic function and biochemical indicators. Thus, this study aimed to elucidate the effects of subchronic cadmium poisoning on insulin and related biochemical indicators in mice.

2. MATERIALS AND METHODS

2.1 Mouse source: ICR mice were purchased from Shenzhen Kozhuo Medical Testing Co., LTD. The experimental animal use license number is SYXK (Su) 2021-0012.

2.2 Feeding and Dosing Methods: Thirty male ICR mice, aged 8 weeks and weighing 36-42 g, were selected as experimental animals for this study. The animals were divided into three groups, with 10 mice in each group: the pure water control group (drinking only pure water for 14 weeks), the $CdCl_2$ low-dose group (drinking water containing 50 mg/L $CdCl_2$ for 14 weeks), and the $CdCl_2$ high-dose group (drinking water containing 200 mg/L $CdCl_2$ for 14 weeks). The corresponding doses of $CdCl_2$ drinking water were prepared, placed in drinking bottles, and placed on appropriate cages. Based on the water intake of the mice, the drinking water was adjusted 2-3 times per week, ensuring continuous water access for 14 weeks, during which normal diet was maintained.

2.3 Feeding management

(1) Housing, Living Conditions, and Environment: Laboratory animals were housed in dedicated cages at a ratio of 3-5 per cage. Each cage was identified by cards marked with test items, animal numbers, and sex. The housing, care, and environment meet the requirements of GB/T 14925-2010 "Environmental and Facilities for Laboratory Animals." Temperature: 19-26℃; Humidity: 40-70%; Lighting: Day and night cycles (lighting hours from 7:00 AM to 7:00 PM).

(2) Feed, water and pollutants: qualified commercial feed was fed daily and drinking water was provided. There was no contamination that affected the test results during feeding and water supply. Feed: sterilized experimental mice maintained feed (full price); drinking water: sterilized pure water.

(3) Animal Medical Care and Health: All animal medical care and health must comply with GVP Good Veterinary Practice. The use and alteration of all anesthetics, sedatives, and other medications must be carried out according to veterinary instructions. This regulation applied to specific drugs, dosages, and dosing intervals. According to current veterinary standards, animals that were injured, sick, or near death require medical care and health maintenance. If they reach a humane endpoint, euthanasia or other measures must be performed. Any decisions made during the trial will appropriately consider the objectives and notify the sponsor.

2.4 Body weight detection: The initial weight was weighed before grouping, and the weight was weighed twice a week (once every 3-4 days), and the final weight was weighed before the end of sampling.

2.5 Blood routine test: The mice were fasted overnight, and blood was taken from the eyeball for EDTA

anticoagulation. Blood routine was measured by an automatic blood analyzer.

2.6 Urinary routine test: Metabolic cage collected the urine of mice 24 hours before death and measured the relevant indicators of urinary routine by urine analyzer.

2.7 Fasting Insulin: Testing in Elisa Mice were fasted overnight, and their eyes were removed for blood collection. Whole blood was collected in 4000 r/min tubes and centrifuged at 10 min to prepare serum. Fasting serum insulin levels were detected using ELISA. The specific steps were as follows: The reagent kit was taken out from the refrigerator 20min in advance and allowed to equilibrate to room temperature. Washed buffer and standard working solution were prepared according to the instructions. Add 100μL of standard and test samples to each well, cover with a membrane, and incubate at 37℃for 90 min. Prepared the biotinylated antibody working solution according to the instructions. Discarded the liquid in each well, shake off any remaining liquid, and add 100μL of biotinylated antibody working solution to each well, mix well, cover with a membrane, and incubate at 37℃ for 60 min. Prepared the enzyme conjugate working solution according to the instructions. Discarded the liquid in each well, add 350 μL of wash buffer to each well, and incubate for 1-2 min. Shake off any remaining liquid from the enzyme conjugate working solution, and repeat this step three times. Add 100μL of enzyme conjugate working solution to each well, cover with a membrane, and incubate at 37℃ for 30 min. Discarded the liquid in each well, shake off any remaining liquid, and wash the plate five times, following the same method as step 6. Added 90 μL of substrate solution to each well, cover with a membrane, and incubate at 37℃ in the dark for 15 min. Add 50 μL of stop solution to each well to terminate the reaction. Immediately measured the absorbance OD values of each well using an ELISA reader at a wavelength of 450 nm. Plot the standard curve using Excel, and calculate the sample concentration values based on the curve equation.

4.6 Biochemical Blood Tests for Glucose, Liver and Kidney Function, and Lipid Profile: Mice were fasted overnight, and their eyes were removed for blood collection. Whole blood was collected at 4000 r/min and centrifuged at 10 min to prepare serum. The serum was analyzed using an automated biochemical analyzer (Pusco MS100) to measure fasting glucose, three renal function parameters (creatinine, urea nitrogen, uric acid), two liver function parameters (ALT, AST), and four lipid profile parameters (TC, TG, HDL-C, LDL-C).

2.7 Ethical Considerations and Animal Welfare: The experiment must comply with animal welfare requirements and meet the ethical review standards for laboratory animals. When designing the experiment, the principle should be followed to optimize the experimental design and minimize the number of animals used. Non-essential animal experiments should not be conducted, and all animal experiments must have valid reasons and valuable purposes. Treat the experimental animals kindly, avoid causing them unnecessary pain, and minimize the intensity of stimuli and shorten the duration of the experiment. During the experiment, sedatives or anesthetics should be administered to alleviate or eliminate the animals suffering. If relief is not achieved, euthanasia should be performed promptly to reduce their distress. Any procedures that may cause pain or harm to the animals should be carried out with care and not in a brutal manner. If fasting or water restriction is necessary for the study, it should only be done for a short period to avoid harming the animals health. For conscious animals, appropriate comfort measures should be taken to reduce their fear and adverse reactions. During surgical procedures, active measures should be taken to ensure the animals receive timely medical care, and euthanasia should be performed at humane endpoints or when the experiment concludes.

2.8 Statistical Methods: A database was established using SPSS20.0 Statistical software and statistical analysis was conducted. For quantitative data, mean ± standard deviation was used for descriptive statistics. ANOVA was employed to compare means among three groups with equal variances, and SLD method was used for pairwise comparisons. Non-parametric tests were applied to compare means among three groups with unequal variances. $P \leq 0.05$ was considered statistically significant.

3. RESULTS

3.1 Effects of cadmium on the weight of mice

The weight of the three groups of mice before intervention was 39.09±1.052g, 38.76±1.936g, 40.34±2.801g, with no statistical difference ($P>0.05$). After cadmium poisoning intervention, the weight of the three groups of mice was compared in the first month, the second month, and the third month after poisoning. The results showed that the average body weight of the three groups of mice increased with the growth of time, but there was no statistical difference between the three groups ($P>0.05$) (Table 1).

Table 1: The weight of three groups of mice at different time periods (X±SD).

Groups	Initial weight	Weight after the first month	Weight after the second month	Weight after three months
Control group	39.09±1.052	47.01±2.700	50.23±3.603	53.21±4.241
$CdCl_2$ Low dose group	38.76±1.936	48.29±1.918	51.87±3.194	52.36±2.140
$CdCl_2$ High dose group	40.34±2.801	47.36±2.599	51.07±2.982	53.21±3.403

3.2 Effects of cadmium on blood routine of mice

Compared with the blank group mice, the blood white blood cells, hemoglobin concentration and hematocrit of the high-dose group mice decreased after 3 months of intervention, while the low-dose group mice were not different from the blank group mice. The other blood routine indexes showed no statistical difference among the three groups (P>0.05), and all blood routine indexes were within the normal range at all times (Table 2).

Table 2: The blood routine in three groups of mice at different time (X±SD).

Index	Control group	$CdCl_2$ Low dose group	$CdCl_2$ High dose group	Reference ranges
WBC	6.45 ± 2.427	6.711 ± 2.165	5.19 ± 1.402	1.05-10.6/10^3/ul
RBC	10 ± 0.899	9.62± 1.141	9.24 ± 0.677	6.7-12.5/10^6/ul
HGB	16.01 ± 1.223	15.4 ± 1.077	13.74 ± 1.077	10.2-16.6/g/l
HCT	47.14 ± 3.939	45.22 ± 3.490	42.05 ± 3.064	32.0-54.0%
MCV	47.13 ± 0.854	47.18 ± 2.116	45.49 ± 1.679	31.0-62.0/fl
MCH	16 ± 0.368	16.07 ± 0.817	14.87 ± 0.574	9.20-20.8/pg
MCHC	34.1 ± 0.316	34.22 ± 0.441	32.7 ± 0.483	220-355/g/dl
RDW	13.96 ± 0.499	14.32± 0.543	13.64 ± 0.493	13.0-23.0%
PLT	855.3±197.779	1014.88 ±241.06	953.2 ± 161.285	400-2300/10^3/ul
PCT	0.328 ± 0.075	0.42± 0.078	0.325 ± 0.063	0.250-1.250%
MPV	3.86 ± 0.401	4.24± 0.564	3.41 ± 0.381	4.5-7.7/fl
PDW	16.72 ± 0.421	17.54 ± 0.786	15.95 ± 0.654	10-18%

Note: white blood cell, WBC;red blood cell,RBC;Hemoglobin,HGB;Red blood cell hematocrit,HCT;Mean red blood cell volume, MCV; Mean hemoglobin,MCH;Mean hemoglobin concentration,MCHC;Red blood cell distribution width, RDW; blood cells, PLT;Platelet Packed Cell Volume,PCT;Mean platelet volume,MPV;Platelet distribution width, PDW.

3.3 Effects of cadmium on routine urinalysis in mice

After 3 months of intervention, compared with the blank group, the creatinine content and β2 microglobulin content in both low-dose and high-dose mice were increased, while other routine urinary indicators showed no statistical difference (P>0.05) (Table 3).

Table 3: The urine test in three groups of mice at different time.

Index	Control group	$CdCl_2$ Low dose group	$CdCl_2$ High dose group
WBC-CELL/ul	negative	iota	iota
ketone bodies-mmol/L	iota	iota	iota
Bilirubin-umol/L	negative	iota	iota
Protein-g/L	iota	iota	iota
Glucose-mmol/L	negative	negative	negative
specific gravity of urine	1.013	1.025	1.025
occult blood test -CELL/nL	negative	negative	negative
PH	6.5	7.1	6.5
Creatinine content (μmol/L)	223.02±41.678	275.80±33.194*	276.77±27.098*
Urinary β2 microglobulin (ng/mL)	6.70±3.054	8.64±5.268	11.985±6.046*

3.4 Effects of cadmium on fasting blood glucose and insulin in mice

We further analyzed the effects of cadmium on fasting blood glucose and insulin in mice. After three months of intervention, compared to the control group, the fasting serum insulin levels in both low and high dose groups were significantly reduced (P<0.01). The higher the cadmium dose, the lower the serum insulin expression. However, there was no statistically significant difference in fasting blood glucose levels among the three groups (P>0.05) (Table 4).

Table 4: The fasting blood glucose and insulin in three groups of mice at different time (X±SD).

Index	Control group	$CdCl_2$ Low dose group	$CdCl_2$ High dose group
Fasting blood-glucose (mmol/L)	6.13±1.081	6.04±1.313	6.06±1.120
Fasting insulin (pg/mL)	290.24±23.919	249.76±5.827	178.32±19.851

3.5 Effects of cadmium on liver and kidney function in mice

To analyze the effects of cadmium on liver and kidney function in mice, we measured the concentrations of alanine aminotransferase, aspartate aminotransferase, creatinine, urea, and urea/creatinine in fasting mice. The results showed that the concentrations of alanine aminotransferase and aspartate aminotransferase in the low and high dose groups were higher than those in the control group, with statistically significant differences

(P<0.05). However, there were no statistically significant differences in the concentrations of creatinine, urea, and urea/creatinine (P>0.05). All these indicators were within the normal range (Table 5).

Table 5: The liver and kidney function in three groups of mice at different time(X±SD).

Index	Control group	$CdCl_2$ Low dose group	$CdCl_2$ High dose group	Reference ranges
Alanine aminotransferase, ALT	60.58±31.355	70.41±16.158	71.83±15.680	28.0-132.0
Aspartate aminotransferase, AST	148.62±65.580	172.10±18.098	158.60±33.435	59.0-247.0
creatinine	61.20±0.749	60.27±0.945	60.02±1.449	18.0-71.0
urea	7.02±1.220	6.25±1.016	7.91±1.050	6.40-10.40
creatinine	28.42±4.979	25.66±3.974	32.71±5.022	/

4. DISCUSSIONS

Cadmium (Cd), as a widespread environmental pollutant and industrial toxin, has garnered significant attention for its harmful effects on human health. The International Agency for Research on Cancer has classified cadmium as a Group 1 carcinogen, confirming its severe threat to human health. In recent years, with the acceleration of industrialization, the problem of cadmium pollution has become increasingly serious, especially in certain industrial clusters and mining areas, where cadmium concentrations in the environment are notably high.[11] This situation has prompted researchers to delve into the toxic mechanisms of cadmium, aiming to develop effective prevention and control strategies.[12,13] In the study of the toxic mechanisms, the relationship between cadmium and diabetes has gained increasing attention. Extensive epidemiological studies and animal experiments have shown that cadmium exposure is closely associated with impaired pancreatic function, insulin resistance, and the development of type 2 diabetes (T2DM). Cadmium can enter pancreatic cells, particularly β cells, causing cytotoxicity, leading to reduced insulin secretion or increased insulin resistance, which in turn results in elevated blood glucose levels. Additionally, cadmium can affect calcium ion metabolism and immunity, further exacerbating damage to the endocrine system. However, despite numerous studies revealing the link between cadmium and diabetes, the specific mechanisms by which cadmium causes diabetes remain unclear.[14,15] Especially under low-dose exposure conditions, different studies often yield varying or even contradictory results.[14] This may be due to differences in experimental design, animal models, exposure duration, and monitoring indicators.[17] Therefore, it is necessary to carry out more systematic and in-depth studies to clarify the specific effects of cadmium on pancreatic function and its mechanism.

In the research of this field, there are still some shortcomings and challenges. First, current studies mainly focus on the direct toxic effects of cadmium on pancreatic cells, while less attention has been paid to how cadmium indirectly damages pancreatic function by affecting other biomolecules or signaling pathways. Second, most epidemiological studies on the relationship between cadmium exposure and diabetes are based on cross-sectional designs, lacking data support from long-term cohort studies, making it difficult to accurately assess the long-term impact of cadmium exposure on the risk of developing diabetes.[18-20] Finally, due to the complexity and widespread nature of cadmium pollution, how to effectively prevent and control cadmium pollution and reduce population exposure levels remains an urgent issue to address.

In response to the aforementioned research deficiencies, this study explored the effects of subchronic cadmium poisoning on insulin and related biochemical indicators in mice through animal experiments. ICR mice were selected as experimental animals and given different doses of cadmium chloride ($CdCl_2$) via drinking water for subchronic poisoning intervention, with a control group receiving only purified water. After a three-month intervention period, we measured the weight, blood routine, urine routine, fasting blood glucose, fasting insulin, and liver and kidney function of the mice to comprehensively evaluate the impact of cadmium on the endocrine system and liver and kidney function in mice.

The findings of this study showed that after 14 weeks of cadmium poisoning intervention, the average body weight of all three groups of mice increased over time, but there was no statistically significant difference between the three groups. This indicates that under the cadmium exposure levels used in this study, cadmium had no significant impact on the growth and development or weight changes of the mice. In terms of blood routine indicators, compared to the control group, the high-dose group showed a decrease in white blood cells, hemoglobin concentration, and hematocrit, while the low-dose group showed no difference compared to the control group. The other blood routine indicators showed no statistically significant differences among the three groups, and all blood routine indicators remained within normal ranges at all time points. This finding aligns with the molecular mechanisms of cadmium-induced anemia reported in 2023.[21] This result suggests that high-dose cadmium exposure may have some effect on the hematological system of the mice, but low-dose exposure has no significant impact. Regarding the effects of cadmium on urine routine: after three months of intervention, compared to the control group, both the

low-dose and high-dose groups showed increased creatinine and β2-microglobulin levels in urine. This suggests that cadmium exposure may lead to impaired kidney function, particularly in the reabsorption function of the renal tubules. In terms of the effects of cadmium on fasting blood glucose and insulin: compared to the control group, both the low-dose and high-dose groups showed a significant decrease in serum insulin levels, and the higher the cadmium dose, the lower the serum insulin expression. However, there was no statistically significant difference in fasting blood glucose levels among the three groups. A similar long-term experiment (6 months) in 2024 showed that continuous cadmium exposure ultimately led to an increase in fasting blood glucose by 18.4%, suggesting that time-dependent effects may play a key role in cadmium toxicity.[22,23]

This result suggests that cadmium exposure may lead to impaired pancreatic function and reduced insulin secretion in mice, although it did not reach the level causing elevated blood glucose in this study. Regarding the effects of cadmium on liver and kidney function in mice: compared to the control group, both low-dose and high-dose groups showed significantly increased concentrations of fasting alanine aminotransferase and aspartate aminotransferase, while there were no statistically significant differences in creatinine, urea, or urea/creatinine levels. This indicates that cadmium exposure may have some impact on liver function in mice, but the direct effect on kidney function was not confirmed in this study.

The results of this study further confirm the detrimental effects of cadmium exposure on islet function in mice, particularly in insulin secretion. Cadmium can significantly reduce fasting serum insulin levels in mice, with a dose-dependent effect. This finding provides experimental evidence for the mechanism by which cadmium causes diabetes, supporting the notion that cadmium affects islet cell function and leads to reduced insulin secretion. Additionally, the study found that cadmium exposure may impair kidney function in mice, as evidenced by increased levels of urinary creatinine and β2-microglobulin. These findings are consistent with previous studies on the nephrotoxicity of cadmium, further confirming its harmful effects on the kidneys. However, it is noteworthy that the direct impact of cadmium exposure on liver function in mice was not significant in this study, which may be related to the experimental design, exposure duration, or choice of monitoring indicators. Future research will further explore the specific impacts of cadmium on liver function and their mechanisms. The results of this study suggest that the potential threat of cadmium pollution to public health cannot be overlooked, especially for those living long-term in areas contaminated with cadmium. Furthermore, this study provides scientific evidence for developing effective strategies to prevent cadmium pollution, helping to reduce human exposure to cadmium and prevent the occurrence of cadmium-related diseases. Finally, this study also offers an experimental foundation and research direction for further exploring the specific mechanisms by which cadmium causes diabetes.

The Limitations and Prospects: this study has some shortcomings. First, only mice were used as experimental animals. Although mice are one of the commonly used animal models, they differ from humans in physiology and metabolism. Therefore, future research should use more types of experimental animals or human cells for experimental validation to enhance the reliability and applicability of the findings. Second, the exposure period in this study was relatively short (14 weeks), which may not fully reflect the long-term effects of cadmium exposure on the endocrine system and liver and kidney functions in mice. Subsequent studies will extend the exposure period to more accurately assess the long-term toxic effects of cadmium. Additionally, there may be limitations in the selection of detection indicators in this study. For example, other biomolecules or signaling pathway indicators related to insulin resistance, such as insulin receptor substrates and phosphatidylinositol-3-kinase, were not detected. These indicators are crucial for understanding the mechanisms of cadmium-induced diabetes. Therefore, future research needs to further improve the detection indicator system to more comprehensively evaluate the impact of cadmium on the endocrine system. Finally, the results of this study suggest that cadmium exposure may cause damage to the endocrine system and liver and kidney functions in mice, but the specific mechanisms are not yet fully understood.[24-26] Future research needs to further explore how cadmium affects pancreatic cell function, disrupts signaling pathways, or causes oxidative stress to lead to endocrine system disorders and liver and kidney dysfunction.

In summary, this study explored the effects of subchronic cadmium poisoning on insulin and related biochemical indicators in mice through animal experiments, achieving certain results. However, there are still many shortcomings and challenges that need to be addressed and further explored in future research. We hope that through sustained efforts and in-depth studies, we can better understand the toxic mechanisms of cadmium, develop effective prevention and control strategies, and protect public health from the threat of cadmium pollution.

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Ethical approval: The study was conducted in accordance with the Declaration of Helsinki, and approved by Research Ethic Committee of Pingshan

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