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# Acute and Subacute Toxicity Evaluation of Corn Silk Extract

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**ABSTRACT:** Many studies have reported therapeutic efficacy of corn silk extract. However, research on its toxicity and safe dose range is limited. Thus, the objective of this study was to determine the acute and subacute toxicity of corn silk extract in ICR mice. To determine acute toxicity, corn silk extract containing high levels of maysin was orally administered to mice at a dose of 0 or 2,000 mg/kg. Clinical symptoms, mortality, and body weight changes were recorded for 14 days. To determine subacute toxicity, corn silk extract was orally administered to mice over a 4-week period, and then body weight, water and food consumption, and organ weight were determined. In addition, urine and serum analyses were performed. In the acute toxicity study, no death or abnormal symptoms was observed in all treatment groups during the study period. Body weights did not show any significant change compared to those of the control group. Lethal dose of corn silk extract was estimated to be more than 2,000 mg/kg. In the 4-week subacute toxicity study, there was no corn silk extract related toxic effect on body weight, water intake, food consumption, urine parameters, clinical chemistry, or organ weight. Histopathological examination showed no abnormality related to the administration of corn silk extract at 500 mg/kg. The maximum non-toxic dose of corn silk extract containing high levels of maysin was found to be more than 500 mg/kg.

**Keywords:** acute toxicity, corn silk, lethal dose, maysin, subacute toxicity

## INTRODUCTION

Herbal medicine attracts a great deal of attention due to its nontoxic nature and traditional use. Nevertheless, many studies have suggested that natural plants might potentially have side effects (1-3). Corn silk, a byproduct of green or yellow maize (*Zea mays* L.), is known to be effective in treating hypertension, nephritis, prostatitis, and urinary tract infections (4). Corn silk extract contains a large amount of maysin, a type of flavonoid specific to corn (5,6). Maysin in corn silk extract is a flavone glycoside containing luteolin, a biologically active substance known to have high antioxidant and anticancer activities (7). Previous studies on maysin have evaluated its anti-obesity, anti-cancer, anti-allergy, anti-oxidant, anti-asthma, and anti-dementia effects (8-10).

When corn silk extract is consumed in excess, there are some side effects such as allergic reactions and stimulation of uterine contraction in rabbits due to unknown toxic substances (11,12). However, the toxicity of corn silk extract has not been explicitly studied. A recent study has reported there is no toxicity to Wistar rats even after they are administered 8% of corn silk extract tea for 90 days (13). Another study evaluated the toxicity of corn silk extract administered to Wistar rats at 100, 200, and 400 mg/kg body weight for 28 days and found no hematological toxicity (14).

If a natural food product is used as a functional food, its safety must be verified first, and its applicability must be approved by the Korean Food and Drug Administration (KFDA). To use corn silk extract in humans, it is important to accurately determine its toxicity (15). Therefore, in this study, we investigated the safety of corn silk extracts including high maysin, and the applicability of corn silk extracts containing high maysin as a functional food material. For this purpose, both 14-d single administration and 4-week repeated oral administration of corn silk extract to mice, in accordance with the KFDA toxicity study guidelines (KFDA Notification No. 2012-86) were performed in this study.

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## MATERIALS AND METHODS

### Sample preparation

Corn silk was collected from the corn named '*Kwangpyeongok*' cultivated by the Korean National Institute of Rural Development. The corn silk was treated with a silk bag before corn silk got pollen on them. The unpollinated corn silks were collected after 3 days of silking, the corn silk was cut into approximately 5 to 10 cm size, and extracted at room temperature with ethanol (Sigma, St. Louis, MO, USA). The process for preparing corn silk extract with high content of maysin was described previously (6). Briefly, corn silk was cut into about 5～10 cm size immediately after harvesting. Then, 2 L of 99% ethanol was added to 1 kg of corn silk and incubated at room temperature for 15 days. The extract was filtered twice and concentrated under reduced pressure at 40°C to obtain corn silk extract. Chlorophyll was removed by adding methylene chloride ($CH_2Cl_2$) 1:1.5 (v:v) to the corn silk extract. The pulverized corn silk extract was again concentrated under reduced pressure. The concentrated corn silk extract was then loaded onto a C18 column to remove carbohydrate and polyphenol materials. As the mobile phase, distilled water was used for carbohydrate removal while 100% ethanol was used for polyphenol removal. From the corn silk extract, active substances including maysin were extracted with distilled water and ethanol as the mobile phase solvent at a flow rate of 20 mL/min for 70 min. The maysin content in the final corn silk extract was 35%. The sample was dried and used in the form of solid powder. The test substance was weighed with an electronic scale on the day of use. It was then added with an excipient to prepare different concentrations (0～50 mg/mL). Corn silk extract, the test substance, was supplied by the Rural Development Administration and National Institute of Crop Science, Republic of Korea. In general, the maysin content in the corn silk extract ranged from 5.2 to 230.5 mg/100 g. However, the content of maysin in the corn silk extract used in this study was 2,783 mg/100 g.

### Animals and diet

Experimental mice were held in a room with controlled conditions (temperature sustained at 19.0～25.4°C, relative humidity of 48.9～70.3%, 12 h of artificial lighting time from 8:00 to 20:00, and illuminance of 150～300 Lux). Mice were provided access to solid rodent chow (LabDiet 5053, Zeigler Bros, Gardners, PA, USA) and filtered purified water. This experiment was conducted in compliance with all regulations applicable to the management and use of laboratory animals. The study was approved by the Medville Animal Experimental Ethics Committee (IACUC) based on provisions of the Animal Protection Act (Law 4379, May 30, 1991, Law 13023, January 20, 2015, and some amendments) (Approval No.: 15-26).

### Acute toxicity study

To determine the acute toxicity of corn silk extract, a single oral dose was used, and the approximate lethal dose (LD) was determined. Twenty-four ICR mice (12 males with body weight of 22.7～23.8 g and 12 females with body weight of 18.3～19.5 g) aged 4 weeks were purchased from NARA Biotech (Seoul, Korea). Six mice of each gender were randomly assigned to the control or test group. For the test group, the administration dose was 2,000 mg/kg of corn extract (10 mL/kg). The individual dose was calculated based on body weight measurements of the day. The animals were given a single intragastric oral administration of corn extract using a disposable syringe (1 mL) equipped with a gastric tube.

Animals were fasted for approximately 3～4 h before administration. Mice were fed 2 h after administration. At 30 min, 1, 2, and 4 h after dosing, animals were monitored for clinical signs and mortality. They were then monitored at least once per day during the 14-d period. Their body weights were recorded before dosing and at 1, 3, 7, and 14 d after dosing. At the end of the observation period, all animals were sacrificed with $CO_2$ gas. Complete gross postmortem analysis was then performed.

### Subacute toxicity study

***Dose administration*:** Twenty-four male ICR mice aged 4 weeks were purchased from NARA Biotech. For the subacute toxicity study, mice were randomly allocated to four groups based on the amount of corn silk extract supplements: control [0 mg corn silk extract/kg body weight (BW)], low dose (5 mg/kg BW), medium dose (50 mg/kg BW), and high dose (500 mg/kg BW). Corn silk extract was orally administered once daily for 4 weeks at a designated time frame. Dosing was performed using a disposable syringe equipped with a gastric tube. For the control group, the same excipient used for dissolution of the corn silk extract was administered.

***Clinical signs and mortality*:** General symptoms of all animals were observed at least once a d for 4 weeks. Mortality and critical conditions were observed twice a day for 4 weeks. Changes in general conditions for a certain period, expression of toxicity, and appearance of abnormal symptoms due to the test substance were observed. Deaths and critical conditions of animals and presence of abnormal signs as well as degree of abnormal signs were recorded separately for each treatment group.

***Body weight, water intake, and food consumption*:** Body weights were measured before administration and once a week after administration as well as on the day of autopsy. However, the weight measured on the day of autopsy was excluded from the body weight assessment as

mice were fasted. Water intake and food consumption were also measured once a week. The average daily intake (g/mouse/d) was calculated by dividing the feed intake by 7 days.

***Urine analysis*:** At four weeks after corn silk extract administration, urine samples were collected using a metabolic cage. Urinalysis was performed using a urine automatic analyzer (CTK Status, Siemens Healthineers, Tarrytown, NY, USA) to examine glucose, bilirubin, ketone body, specific gravity, pH, protein, and occult blood.

***Serum biochemistry*:** All animals were fasted for at least 3 h on the day of autopsy. They were then anesthetized with isoflurane. Blood collected from a canine vasculature was centrifuged at 3,000 rpm for 10 min. Serum was analyzed with a blood biochemical analyzer [Hitachi 7020 (Hitachi, Ltd., Tokyo, Japan) and PDC-800 (Fujifilm, Tokyo, Japan)] to measure the levels of aspartate aminotransferas, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen, creatinine, creatine phosphokinase (CPK), glucose, total protein, albumin, albumin/globulin ratio, total cholesterol, triglyceride, inorganic phosphorus, calcium ion, sodium ion, potassium ion, and chloride ion.

***Histopathological examination*:** After 4 weeks of corn silk extract administration, prior to autopsy, all animals were fasted for 18 h. For all autopsied animals, the tissues or organs (brain, heat, liver, spleen, lung, kidney, testis, epididymis, and prostate) were removed and weighed. The samples were fixed in 10% natural buffered formalin, and then subjected to general tissue treatments such as dehydration and paraffin embedding. Tissue sections were cut and hematoxylin and eosin staining was performed. Histopathologic examination under light microscope was performed on tissues and organs of all individuals in the control and high dose groups.

### Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 16 (SPSS Inc., Chicago, IL, USA). Data are expressed as mean and standard deviation. After verifying the homogeneity of variance using Levene Test, one-way analysis of variance (ANOVA) was conducted. When significant homogeneity was confirmed, Scheffe post-test was performed. If homogeneity of variance was insignificant, Dunnett's T3 test was performed. Statistical significance was considered when two tailed *P*-value was less than 0.05.

## RESULTS

### Acute toxicity study

During the 14-d test period, there was no statistically significant difference in body weight between the control and the corn silk extract (2,000 mg/kg) treatment group (Table 1). No mortality or abnormal finding at necropsy was observed for the control or the corn silk extract (2,000 mg/kg) treatment group (data not shown).

### Subacute toxicity study

After observing body weight changes for 4 weeks, animals in both the control group and corn silk extract treated groups showed increase in their body weights at a normal rate, proving that corn silk extract administration had no significant effect on body weight changes. Mean water intake and food consumption were not significantly different between the control group and the corn silk extract treated groups during the test period (Table 2). In the urine analysis, there was no significant difference in any test variable (glucose, bilirubin, ketone body, specific gravity, pH, protein, and occult blood) between the control group and corn silk extract treated groups (Table 3).

Serum biochemical markers in corn silk extract treated groups were not significantly different from those of the control group (Table 4). When weights of organs such as brain, heart, liver, spleen, kidney, lung, testis, epididymis, and prostate in the corn silk extract treated groups were compared to those of the control group, no significant difference was found (Table 5). No significant histopathological changes were observed in all of the tissues or organs at either dose of combination of corn silk extracts, even at even at the high dose (500 mg/kg) with

**Table 1.** Mean body weight of male and female rats fed corn silk extract in acute toxicity study (unit: g)

| Parameter | Body weight changes at days after corn silk extract treatment | | | | | |
|---|---|---|---|---|---|---|
| | 0 d | 1 d | 3 d | 7 d | 14 d | Weight gain |
| Male | | | | | | |
| 0 (control) | 29.3±1.2[1)] | 29.9±1.5 | 31.2±1.7 | 32.5±2.3 | 34.7±2.6 | 5.4±1.6 |
| 2,000 mg/kg[2)] | 28.9±1.8 | 29.6±1.9 | 30.9±2.8 | 32.9±3.1 | 35.1±2.8 | 6.1±1.2 |
| Female | | | | | | |
| 0 (control) | 22.6±0.6 | 23.8±0.8 | 24.5±0.7 | 25.5±0.7 | 26.2±0.4 | 3.6±0.4 |
| 2,000 mg/kg | 23.2±0.5 | 23.5±1.3 | 24.8±1.1 | 26.1±1.0 | 27.2±1.3 | 4.1±0.8 |

[1)]Data are presented as mean±SD (n=5 in each group, $P>0.05$ for all comparisons between corn silk extract treated groups and control group).
[2)]The dose of corn silk extract was set at either 0 or 2,000 mg/kg body weight.

**Table 2.** Mean body weight gain, food consumption, and water intake of rats fed corn silk extract in subacute toxicity study

| Parameter | Dose of corn silk extract (mg/kg body weight) | | | |
|---|---|---|---|---|
| | 0 (control) | 5 | 50 | 500 |
| Initial body weight (g) | 29.3±4.8[1)] | 29.6±0.9 | 29.3±0.8 | 29.0±1.0 |
| Final body weight (g) | 34.5±2.7 | 35.0±1.8 | 35.1±2.1 | 34.1±1.1 |
| Total weight gain (g) | 5.2±1.9 | 5.3±1.1 | 5.8±1.4 | 5.1±0.5 |
| Mean food consumption (g/d) | 6.7±0.7 | 6.1±0.5 | 6.5±0.6 | 6.0±0.6 |
| Mean water consumption (g/d) | 6.7±0.7 | 6.8±0.5 | 6.3±0.4 | 6.5±1.0 |

[1)]Data are presented as mean±SD (n=5 in each group, $P>0.05$ for all comparisons between corn silk extract treated groups and the control group).

**Table 3.** Summary of urine analysis for rats fed corn silk extract in subacute toxicity study

| Parameter | | Dose of corn silk extract (mg/kg body weight) | | | |
|---|---|---|---|---|---|
| | | 0 (control) | 5 | 50 | 500 |
| Volume (mL) | Mean±SD | 1.50±0.7[1)] | 1.54±1.09 | 1.30±0.32 | 1.58±0.74 |
| Glucose | Negative | 4[2)] | 5 | 4 | 4 |
| | Trace | 1 | | 1 | 1 |
| Bilirubin | Negative | 5 | 5 | 4 | 5 |
| | 1+ | | | 1 | |
| Ketone body | Negative | | | | |
| | Trace | 1 | 4 | 2 | 3 |
| | 1+ | 4 | 1 | 3 | 2 |
| Specific gravity | ≤1.005 | | | | |
| | 1.010 | 2 | | | |
| | 1.015 | | 3 | 2 | 1 |
| | 1.020 | 1 | 1 | 2 | 2 |
| | 1.025 | 1 | | 1 | 2 |
| | ≥1.030 | 1 | 1 | | |
| Occult blood | Negative | 5 | 3 | 5 | 4 |
| | Trace intact | | 1 | | |
| | Trace lysed | | 1 | | |
| | 1+ | | | | 1 |
| Protein | Negative | | | | |
| | Trace | | | | |
| | 1+ | 2 | 4 | 2 | 3 |
| | 2+ | 3 | 1 | 3 | 2 |
| pH | 6.5 | | | | |
| | 7.0 | 3 | 1 | 1 | 2 |
| | 7.5 | 1 | 2 | | 1 |
| | 8.0 | | | | |
| | 8.5 | | | 3 | |
| | ≥9.0 | 1 | 2 | 1 | 2 |

[1)]$P>0.05$ for all comparisons between corn silk extract treated groups and the control group (n=5 in each group).
[2)]Number of animals examined.

respect to control. Mortality or abnormal symptoms were not observed in either the control group or corn silk extract treated groups (data not shown). Therefore, administration of corn silk extract at a dose up to 500 mg/kg did not show any toxicity.

## DISCUSSION

Recently, improvements in living standards and medical technology have led to increased researches to develop food and pharmaceutical products using natural products. However, safety of functional plant foods is of concern to consumers. Functional plant foods may have toxic effects on health when misused. Therefore, it is essential to confirm their safety through acute and subacute toxicity tests before commercializing functional plant foods to humans.

General toxicity tests measures changes in toxicity depending on dose and time after administration of test substances (16). To examine the toxicity of a test substance, the toxicity of the test substance to all organ tis-

**Table 4.** Summary of blood biochemical analysis in rats fed corn silk extract in subacute toxicity study

| Parameter | Dose of corn silk extract (mg/kg body weight) | | | |
|---|---|---|---|---|
| | 0 (control) | 5 | 50 | 500 |
| AST (IU/L) | 75.0±9.0[1)] | 71.0±12.0 | 62.0±12.0 | 61.0±21.0 |
| ALT (IU/L) | 32.0±16.0 | 40.0±8.0 | 32.0±10.0 | 29.0±4.0 |
| ALP (IU/L) | 257.0±23.0 | 299.0±82.0 | 255.0±54.0 | 242.0±48.0 |
| BUN (mg/dL) | 15.0±7.0 | 21.0±4.0 | 17.0±1.0 | 18.0±2.0 |
| CRE (mg/dL) | 0.3±0.1 | 0.3±0.1 | 0.3±0.0 | 0.3±0.0 |
| CPK (IU/L) | 236.0±206.0 | 78.0±33.0 | 63.0±15.0 | 66.0±59.0 |
| GLU (mg/dL) | 205.0±37.0 | 228.0±31.0 | 210.0±14.0 | 183.0±65.0 |
| TP (g/dL) | 6.3±0.5 | 6.4±0.3 | 6.3±0.1 | 5.9±0.4 |
| ALB (g/dL) | 2.0±0.2 | 2.1±0.1 | 2.0±0.1 | 1.9±0.1 |
| A/G (ratio) | 0.48±0.02 | 0.47±0.02 | 0.48±0.02 | 0.47±0.02 |
| CHO (mg/dL) | 130.0±18.0 | 151.0±17.0 | 153.0±9.0 | 140.0±18.0 |
| TG (mg/dL) | 93.0±24.0 | 69.0±17.0 | 79.0±23.0 | 74.0±9.0 |
| IP (mg/dL) | 9.93±0.91 | 9.64±0.87 | 10.04±1.57 | 9.04±0.95 |
| Ca (mg/dL) | 9.9±0.6 | 10.2±0.6 | 9.8±0.3 | 9.6±0.4 |
| Na (mmol/L) | 148.0±1.0 | 146.0±1.0 | 149.0±1.0 | 149.0±1.0 |
| K (mmol/L) | 7.2±0.4 | 7.1±0.1 | 7.0±1.2 | 6.1±0.7 |
| Cl (mmol/L) | 117.0±1.0 | 115.0±2.0 | 118.0±1.0 | 117.0±1.0 |

[1)]Data are presented as mean±SD (n=5 in each group, $P>0.05$ for all comparisons between corn silk extract treated groups and the control group).
AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CRE, creatinine; CPK, creatine phosphokinase; GLU, glucose; TP, total protein; ALB, albumin; A/G, albumin/globulin ratio; CHO, total cholesterol; TG, triglyceride; IP, inorganic phosphorus.

**Table 5.** Summary of relative organ weight[1)] changes (%) in rats fed corn silk extract in subacute toxicity study

| Parameter | Dose of corn silk extract (mg/kg body weight) | | | |
|---|---|---|---|---|
| | 0 (control) | 5 | 50 | 500 |
| Brain | 1.43±0.09[2)] | 1.46±0.07 | 1.48±0.05 | 1.52±0.15 |
| Heart | 0.5±0.03 | 0.49±0.02 | 0.51±0.03 | 0.49±0.03 |
| Liver | 5.52±0.98 | 5.33±0.26 | 5.09±0.38 | 5.27±0.63 |
| Spleen | 0.43±0.04 | 0.44±0.09 | 0.46±0.05 | 0.44±0.06 |
| Kidney (left) | 0.79±0.08 | 0.79±0.05 | 0.75±0.04 | 0.74±0.08 |
| Kidney (right) | 0.79±0.11 | 0.85±0.05 | 0.8±0.02 | 0.79±0.06 |
| Lung | 0.65±0.06 | 0.69±0.12 | 0.70±0.07 | 0.66±0.05 |
| Testis (left) | 0.35±0.03 | 0.30±0.02 | 0.35±0.03 | 0.35±0.01 |
| Testis (right) | 0.37±0.03 | 0.35±0.02 | 0.36±0.03 | 0.36±0.02 |
| Epididymus (left) | 0.17±0.02 | 0.14±0.02 | 0.15±0.01 | 0.16±0.02 |
| Epididymus (right) | 0.16±0.02 | 0.16±0.02 | 0.15±0.02 | 0.14±0.02 |
| Prostate | 0.05±0.02 | 0.04±0.02 | 0.04±0.02 | 0.03±0.02 |

[1)]Relative organ weight=(organ weight/28-d body weight)×100.
[2)]Data are presented as mean±SD (n=5 in each group, $P>0.05$ for all comparisons between corn silk extract treated groups and the control group).

sues needs to be assessed by acute and subacute toxicity tests using laboratory animals. Acute toxicity tests, also known as single dose toxicity tests, can qualitatively and quantitatively evaluate toxicity that occurs within a short period when a test substance is administered to a test animal in a single dose. Subacute toxicity tests, also known as 4-week dose range finding toxicity tests, measure the toxicity changes after repeated administration of the test substance to the test animal depending on dose and time (17).

In this study, both acute and subacute toxicity tests were performed to obtain applicable safety dose range data for corn silk extract. In the acute toxicity test, results showed no significant difference in body weight change between the corn silk extract treated group and the control group. There was no death resulting from the administration of corn silk extract in all experimental groups. The $LD_{50}$ of the test substance was also estimated to be over 2,000 mg/kg.

For 4 weeks of the subacute toxicity test, the highest dose for corn silk extract was chosen to be 500 mg/kg instead of 2,000 mg/kg. This is because it is difficult to

obtain a high maysin content in the corn silk extract in sufficient amounts. The concentration of maysin in corn silk extract used in this study was more than 10 times higher than the amount of maysin found in normal corn silk extract. Such dose of maysin administered in this study is well above the average dose administered in other experiments (6,13,14,18).

Previous studies have reported that administration of corn silk extract containing normal levels of maysin had no significant toxic effects on experiment animals regardless of whether the extract was used at a dose less than 500 mg/kg body weight or more than 500 mg/kg body weight (13,14). Likewise, Wang et al. (13) have shown that feeding corn silk extract (at levels up to 8.0% in diet) to rats for 90 days does not affect their body weight or feed intake. In another study, 1∼4% corn silk extract intake for 72 h had no toxic effect in Wister rats (18). Our findings also showed that corn silk extract at dose up to 500 mg/kg is safe.

In this study, urine analysis results for the corn silk extract treatment groups were not significantly different from those of the control group. Out of all parameters tested in the urine analysis, ketone bodies showed a slight increase corresponding to the increased dose of corn silk extract. However, the amount of ketone bodies detected was minimal, showing no association with changes in body weight or blood biochemical parameters. Thus, it can be concluded that the increase of ketone bodies in groups treated with corn silk extract is not an index of toxicity due to the corn silk extract.

Feeding a diet containing corn silk extract at a dose up to 500 mg/kg to mice for 4 weeks had no adverse effects on blood biochemical parameters. CPK levels were decreased in mice treated with corn silk extract compared to those in the control group. However, the decrease was not statistically significant. This is probably because two mice in the control group showed relatively high CPK values, resulting in relatively high mean CPK value for the control group. There were no abnormal findings associated with CPK levels in corn silk extract treated groups such as water intake or urine analysis. Therefore, it is reasonable to conclude that the administration of the test substance is not responsible for the low CPK level found in the treatment group.

Levels of blood glucose and triglycerides in mice fed the corn silk extract seemed to decrease compared to those of the control group, but the decrease was not statistically significant. This result is not consistent with previous studies showing that the aqueous extraction of corn silk extract can lead to significant decreases in blood glucose among alloxan-induced hyperglycemic rat via increasing insulin levels and improving function of pancreatic β-cells (10). Cha et al. (19) showed that serum glucose and triglyceride levels in the corn silk extract treated group are significantly lower than those of the control group. They also found that improvements of these parameters in the control group were associated with elevated mRNA expression levels of adipocytokines (19). Discrepancies in the results may be due to differences in the types of experimental animals, treatment methods (injection or feeding), or the duration of the experiment. Further studies are needed to clarify the role of corn silk extract in treating or preventing diseases such as diabetes or dyslipidemia.

The results of this study show that corn silk extract had no significant effect on relative organ weights of mice. It has been generally accepted that corn silk extract is effective in treating kidney related diseases as a diuretic agent. It has been hypothesized that corn silk extract contains many phytochemicals that can provoke diuresis (20). The diuretic action of corn silk extract may result in increased kidney weight because rapid absorption of corn silk extract by the small intestine with rapid release into urine can lead to overload of the kidneys (21). Therefore, if corn silk extract at the amount used in this study causes toxicity, it might be due to changes in kidney weight, blood urea levels, and urinary parameters. These are known markers of renal dysfunction. Results of this study showed no diuretic effect of corn silk extract as blood Na levels and K levels (markers of toxicity to kidney) in mice fed 500 mg/kg of corn silk extract. This result is consistent with results from other studies showing that corn silk extract at a dose of 500 mg/kg body weight does not affect proximal tubular function or uric acid excretion (18). In conclusion, no death or abnormal findings in the acute and subacute studies were observed, and the subacute toxicity test using 500 mg/kg of corn silk extract to treat male ICR mice for 4 weeks resulted in no toxicological changes.

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## AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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