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***Original Research Article***

# Therapeutic and Overdose Effects of Camel Urine in Male Wistar Rats

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ABSRTACT

Camel urine is used in northern Nigeria as a therapeutic option for treatment of various human illnesses. Local traditional medical practitioners prescribe therapeutic dosages for the use of camel urine; however, such dosages are arbitrarily given and not based on research findings. A subacute oral toxicity study of camel urine was conducted in male Wistar rats. Thirty (30) healthy male Wistar rats were grouped into three (10 rats/group) and administered camel urine orally for two weeks. Group 1 (control) was administered distilled water orally at 2ml/kg body weight. Group 2 and 3 were administered camel urine at Human Therapeutic Dose Equivalent (TD) and Twice the Human Therapeutic Dose Equivalent (2TD), respectively. Food and water consumption, body weight, serum biochemical indices, serum electrolytes, haematological indices, and organ histological changes were determined. The results indicated a significant decrease in leucocyte count, platelet count, and levels of serum total bilirubin, direct bilirubin, glucose, urea, sodium, and chloride in the 2TD group. Both the TD and 2TD groups exhibited a decrease in food consumption and blood total bilirubin concentrations compared to the control group. However, no histopathological changes were observed in any of the organs (liver, kidney, heart, lungs, spleen, intestine, stomach and testis) examined. The, oral administration of camel urine at twice the therapeutic dose (2TD) resulted in a decrease in food consumption and platelet count, and it may also suppress the immune system by reducing the leucocyte count in rats.

**Keywords:** Camel, Urine, Oral, Therapeutic Dose, Overdose, Rat

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## Introduction

Camel urine has traditionally been used to treat various human illnesses, particularly in the Middle East and North Africa. In northern Nigeria, it is well-known as a natural therapeutic product, likely owing to its cultural significance, accessibility, and affordability when compared to conventional medications. It is used to treat infectious diseases, diabetes, and cancer. This practice is backed by findings indicating that camel urine possesses significant potential health benefits.[1-4] Studies have demonstrated that camel urine exhibits antibacterial, antifungal, antiviral, and antioxidant properties.[5-7] According to Al-Ghumlas *et al*.[8] camel urine counteracts methotrexate hepatotoxicity and demonstrates cytoprotective, antiapoptotic, antioxidative, antihyperglycaemic, and antithrombotic effects in rats. Furthermore, a study indicated that camel urine exhibits a hepatocurative effect on hepatotoxicity induced by carbon tetrachloride in albino rats.[9] It also possesses a strong ulcer-healing effect in cases of indomethacin-induced gastric damage.[10]Studies have demonstrated the anticancer effects of camel urine,which are linked to its ability to inhibit cancer cell proliferation, induced apoptosis in cancer cells, eliminate malignant tumours in various organs, and hinder the progression to metastasis.[2,11-13] The antiplatelet activity of camel urine has also been reported.[14]

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Regarding its toxicity, there are few reports available concerning the effects of camel urine. Existing studies indicate that the administration of camel urine in moderate dosages does not result in adverse effects in rats.[2,10] However, there is insufficient information regarding the safety of camel urine at therapeutic dosages in rats.

## Materials and Methods

*Chemicals and reagents*

All chemicals and reagents were of high purity. Ketamine and xylazine were products of Sigma-Aldrich. Test kits for biochemical assays were products of Agape Diagnostics (Switzerland). The chemicals and reagents were purchased from major dealers in Nigeria.

*Collection of camel urine samples*

Fresh camel urine samples were purchased in lidded containers from major retailers in the Abattoir Market, Dala Local Government, Kano State, Nigeria. The urine samples were kept at ambient temperature away from light to avoid any possible oxidation until used.

*Experimental animals*

Healthy male Wistar albino rats were obtained from the National Veterinary Research Institute (NVRI), Vom, Jos, Plateau State, Nigeria. The animals were allowed to acclimatise for a period of one week. The animals were housed in polypropylene cages on hardwood chip bedding in a ventilated environment with a 12-hour light and dark cycle at a temperature of 24-25 °C. The animals had free access to food and water. The research was approved by the Institutional Animal Care and Use Committee (IACUC) of Modibbo Adama University Yola with reference number MAU/FLS/2023/031 in line with the National Institutes of Health Guideline for the care and utilisation of laboratory animals.[15]

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*Experimental design*
Thirty (30) male Wistar rats were allocated to three (3) groups (10 rats/group). Group 1 (control) was administered distilled water orally at 2 ml/kg body weight. Groups 2 and 3 were administered camel urine orally at 1.5 ml/kg and 3 ml/kg, corresponding to the human therapeutic dose (TD) and twice the human therapeutic dose (2TD), respectively, over a duration of two weeks. The human therapeutic dosage for camel urine in adults is estimated at 100 ml per day. The TD dosage was converted to an animal equivalent dose for rats by employing the formula for the human equivalent dose (HED).[16] The animals were observed daily throughout the experimental period for signs of toxicity.

Animal grouping and treatment

| Group | Treatment |
|---|---|
| Group 1 (control) | Administered distilled water (2 ml/kg) orally only. |
| Group 2 | Administered camel urine at Human therapeutic dose equivalent (TD). |
| Group 3 | Administered camel urine at twice the Human therapeutic dose equivalent (2TD). |

*Blood sample collection*
On day 14, food was withdrawn overnight, but the animals were given free access to water. The animals were anaesthetised using xylazine and ketamine administered via intraperitoneal injection. Xylazine was administered at 5 mg/kg, while ketamine was administered at 90 mg/kg.[17] Blood samples were obtained through cardiac puncture.

*Determination of animal body weight*
Animal body weights were recorded at the start of the experiment and subsequently measured on a weekly basis using a weighing balance.

*Determination of food consumption*
Food consumption for each cage was measured daily by calculating the difference between the quantity of food added and the amount of food remaining in each cage after a 24-hour period.

*Determination of water consumption*
Water consumption for each cage was measured daily by calculating the difference between water provided for each cage (ml) and remaining (ml) after 24 hours.

*Determination of serum biochemical Indices*
Blood samples for serum biochemistry were collected in plain tubes without anticoagulant. The blood samples were allowed to coagulate for about twenty minutes, followed by centrifugation at 6000 rpm for ten (10) minutes for separation of serum. Serum concentrations of creatinine, urea, protein, albumin, direct bilirubin, total bilirubin, and glucose, along with the activities of alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase, were measured using test kits obtained from Agape Diagnostics (Switzerland). The serum electrolytes calcium (Ca), sodium (Na), potassium (K), and chloride (Cl) were assayed using an automated electrolyte analyser (KH-996, Kinghawk).

*Determination of haematological indices*
Blood samples were collected in EDTA (ethylene diamine tetra-acetic acid) containers. An automated haematologyanalyser (RT-7200) was used to determine erythrocyte count, haemoglobin, packed cell volume, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, leucocyte count, neutrophils, lymphocytes, monocytes, eosinophils, basophils and platelets.

*Histological examination*
The histological analysis of tissues was performed using conventional techniques.[18] Briefly, the heart, intestines, kidneys, liver, lungs, spleen, stomach, and testis were carefully removed and prepared for photomicrographic examination. The tissues were fixed in 10% buffered neutral formalin. They were kept in the fixative for 12 hours, and then they were dehydrated by going through a series of ethanol cycles that went from 70% to absolute ethanol and then fixed in paraffin. The tissue was cut into 5-µm slices and deparaffinised and stained with Mayer's haematoxylin and eosin stains and examined under a light photomicroscope.

*Statistical analysis*
Results were expressed as mean ± standard error . Statistical data were analysed using a one-way analysis of variance (ANOVA) (SPSS 24.0). Treatment groups were compared with the control using Dunnett's tests. For all comparisons, p-values less than 0.05 were considered statistically significant.

## Results and Discussion

Safety evaluation studies are conducted on drugs and natural products to identify the potential risks to consumers. Sufficient information is available about the therapeutic value of most natural products including camel urine, but little is known on their toxicity. In this study, a two week repeated dose toxicity study of camel urine was evaluated in Wistar rats following therapeutic and overdose exposures.

*Clinical signs*
None of the animals from the control group or camel urine-treated groups showed any signs of toxicity. All the animals survived to the end of the study.

*Changes in body weight and food and water consumption*
Table 1 shows the therapeutic and overdose effects of camel urine on animal body weight. A decrease in body weight gain is considered as an indicator of toxicity.[19-20] In this study, the body weights of animals in the control group are similar to those in the TD and 2TD groups, suggesting that the health condition of rats was not affected. The animals in the TD and 2TD groups had significantly lower food consumption when compared with the control group (Figure 1). The reduction in food consumption was observed in the initial week (week 1) and continued to the last week (week 2). Low food consumption is usually linked to adverse effects caused by toxic chemicals.[21-22] Alternatively, low food consumption may be caused by decreased appetite. In contrast, no alterations were seen in the water consumption of rats administered camel urine at TD and 2TD at both week 1 and week 2 (Figure 2).

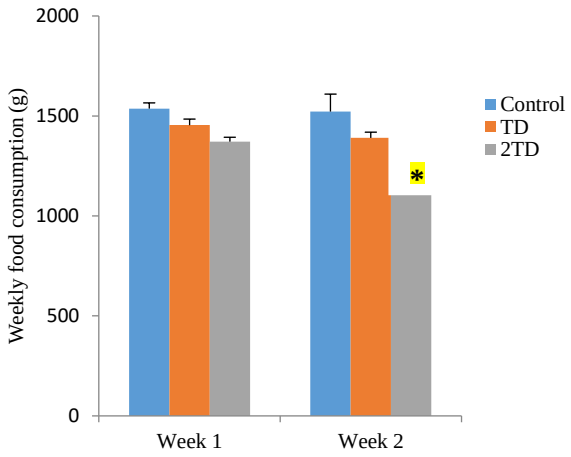


**Figure 1:** Therapeutic and overdose effects of camel urine on food consumption of rats; *****significantly different compared to the control group ($p < 0.05$).

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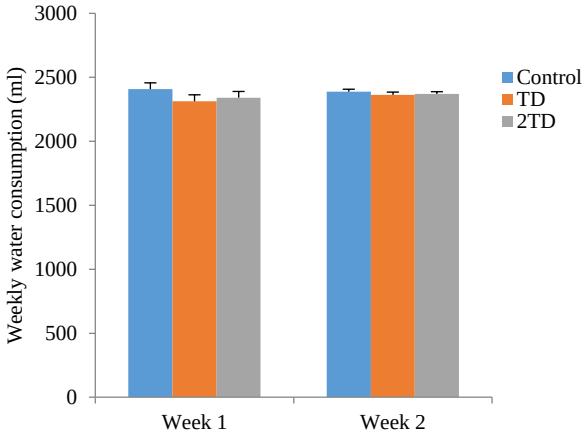


**Figure 2:** Therapeutic and overdose effects of camel urine on water consumption of rats. There is no significant ($p > 0.05$) difference in food consumption between the groups administered camel urine (TD and 2TD) and the control group**.**

**Table 1:** Therapeutic and overdose effects of camel urine on animal weight gain

| Group | Initial | Week 1 | Week 2 | Weight gain (%) |
|---|---|---|---|---|
| Control | 204.10 ±15.62 | 225.49 ±19.89 | 221.33 ±16.70 | 8.44 |
| TD | 206.78 ±12.94 | 224.07 ±19.98 | 224.38 ±19.61 | 8.51 |
| 2TD | 204.59 ±13.41 | 210.33 ±21.59 | 217.59 ±27.08 | 6.35 |

Values are mean ± standard error; n=10; TD, therapeutic dose; 2TD, twice therapeutic dose.

*Serum biochemistry*

Table 2 shows the therapeutic and overdose effects of camel urine on some serum biochemical indices in rats. There was a significant decrease in the levels of serum total bilirubin in the TD and 2TD groups while the level of serum direct bilirubin decreased only in the 2TD group. Elevated levels of bilirubin are related to hepatic injury or increased break down of erythrocytes.[23] The observed reduction in serum bilirubin levels in the TD and 2TD groups was considered a pharmacological effect that may enhance the liver's ability to clear bilirubin through the hepatobiliary tract. This result may validate the claims for the use of camel urine in the treatment of liver diseases.[2,6]

A significant decrease in serum urea, sodium and chloride concentrations in TD and 2TD groups were observed. Alterations in serum levels of these parameters are related to kidney function.[24] However, the serum level of creatinine, which is considered the most sensitive indicator of renal function, remained unchanged, indicating a subtle effect on the kidney.[25-26] However, the concentrations of other biochemical indices in the TD and 2TD were not altered.

Additionally, administration of camel urine decreased serum glucose levels in the 2TD group. Previous studies have shown that camel urine possess antiglycaemic properties and antidiabetic properties.[3] The reduction in blood glucose levels highlights the hypoglycaemic properties of camel urine and supports the established claims regarding its antidiabetic potential.

**Table 2**: Therapeutic and overdose effects of camel urine on some serum biochemical indices in rats

| Parameters | Control | TD | 2TD |
|---|---|---|---|
| Total protein (g/dl) | 5.49±0.43 | 5.88±0.05 | 5.81±0.06 |
| Albumin (g/dl) | 3.81±0.09 | 4.04±0.03 | 4.01±0.12 |
| TBIL (µmol/L) | 0.73±0.07 | 0.55±0.04* | 0.45±0.02* |
| DBIL (µmol/L) | 0.21±0.02 | 0.17±0.01 | 0.41±0.03* |
| Glucose (mmol/L) | 4.84±0.21 | 5.10±0.22 | 2.86±0.03* |
| Urea (mg/dl) | 51.85±0.62 | 52.18±0.49 | 48.88±0.91* |
| Creatinine (mg/dl) | 0.97±0.01 | 0.90±0.03 | 0.89±0.02 |
| Sodium (mmol/L) | 138.12±0.12 | 136.28±0.61 | 133.34±1.25* |
| Potassium (mmol/L) | 5.50±0.14 | 5.97±0.20 | 5.52±0.09 |
| Chloride (mmol/L) | 103.77±0.25 | 103.40±0.26 | 102.19±0.38* |
| Calcium (mmol/L) | 1.28±0.02 | 1.25±0.06 | 1.24±0.01 |
| ALT (U/L) | 30.19±1.61 | 29.26±2.42 | 28.14±0.36 |
| AST (U/L) | 109.37±2.25 | 118.43±1.33 | 118.49±4.72 |
| ALP (U/L) | 140.20±6.98 | 154.13±4.62 | 157.39±3.85 |

Values are mean ± standard error; n=10; *****significantly different compared to the control ($p < 0.05$);TD, therapeutic dose; 2TD, twice therapeutic dose; TBIL, total bilirubin; DBIL, direct bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

*Haematological indices*

Evaluation of the haematological indices showed some alteration in leucocyte counts and platelet counts (Table 3). Camel urine at twice the therapeutic dose (2TD) significantly decreased the leucocyte count. The reduction in leucocyte count may compromise the immune system.[27] This finding is in contrast with previous reports that demonstrated that camel urine has immunostimulatory effect.[2] The observed differences in the two reports were ascribed to the high dosage used in the present study.

Additionally, the platelet levels in the 2TD group showed a significant decrease when compared to the control group. Decreased in platelets levels are due to reduced production and or destruction of platelets in the body.[28] The significant decrease in platelet counts suggest that the extract could reduce the effectiveness of the blood clotting processes, resulting in thrombocytopenia.

*Histophatological changes*

Histopathological examinations of the liver, kidneys, heart, lungs, spleen, testis, intestine and stomach from control, TD and 2TD groups showed no structural alterations in the organs (Figure 3). This is consistent with current observations on biochemical and haematological indices that demonstrate the safety of camel urine, especially at the therapeutic exposure.

**Table 3:** Therapeutic and overdose effects of camel urine on haematological indices in rats

| Parameter | Control | TD | 2TD |
|---|---|---|---|
| Erythrocyte count (x $10^{12}$/L) | 7.36 ± 0.20 | 6.85 ± 0.15 | 7.29 ± 0.40 |
| Packed cell volume (%) | 46.44 ± 1.30 | 43.91 ± 0.87 | 48.84 ± 3.19 |
| Haemoglobin (g/dl) | 16.86 ± 0.47 | 15.91 ± 0.32 | 16.80 ± 0.87 |
| MCV (fl) | 63.30 ± 0.73 | 64.20 ± 0.20 | 63.80 ± 0.63 |
| MCH (pg) | 22.84 ± 0.25 | 23.21 ± 0.05 | 23.06 ± 0.10 |
| MCHC (g/dl) | 36.16 ± 0.07 | 36.12 ± 0.07 | 36.22 ± 0.44 |
| Leucocyte count (x $10^9$/l) | 13.14 ± 0.74 | 11.27 ± 0.63 | 10.04 ± 0.40* |
| Platelet count (x $10^9$/l) | 453.40±12.37 | 458.30 ± 22.37 | 350.90 ± 33.99* |

Values are mean ± standard error; n=10; *****significantly different compared to the control ($p < 0.05$); TD, therapeutic dose; 2TD, twice therapeutic dose; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration

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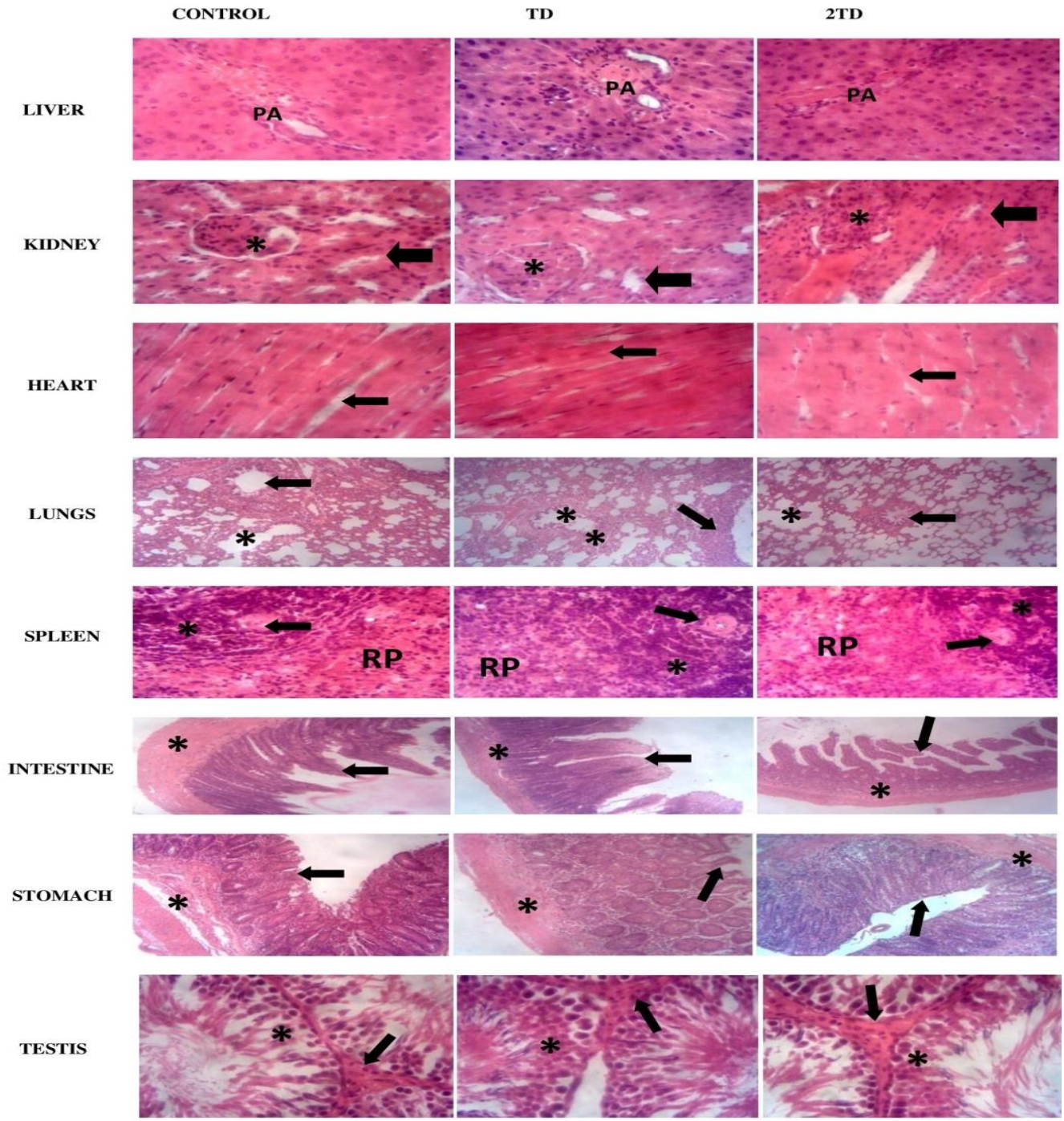


**Figure 3:** Photomicrographs of tissues from the control group, the therapeutic dose (TD) group, and twice the therapeutic dose (2TD) group showing the liver with apparently normal portal areas (PA);kidney with normal glomerulus (asteriks) and renal tubular epithelium (arrows); heart with normal myofibres (arrows); lungs with normal alveoli (asteriks) and bronchiolar epithelium (arrows); spleen with normal lymphoid follicles (asteriks) with central arteriole (arrows) and red pulp (RP);small intestine with normal mucosal villi (arrows)and submucosa (asteriks);stomachwith apparently normal mucosa (arrows) and submucosa layers (asteriks) and thetestis showing normal seminiferous germinal epithelium (asteriks) and interstitium (arrows). H and E stain × 400.

## Conclusion

Administration of camel urine at the therapeutic dose (TD) caused no adverse effects in rats. This indicates that camel urine is safe when consumed at the current therapeutic dosage. The findings support the administration of camel urine at the TD dosage for the management of various human illnesses. However, consumption of camel urine above the therapeutic dosages may suppress the immune system and reduce the ability for blood clotting in rats and possibly in humans.

## Conflict of interest

The authors declare no conflict of interest

### Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

### Acknowledgements

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