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The Physiological Effects of Caffeine on Kidney Function Parameters in Male Wistar Rats

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ABSTRACT

The present study examined the impact of caffeine on renal biochemical parameters in male Wistar rats. A total of twenty-five animals were allocated at random into five equal groups: one vehicle control and four caffeine-treated cohorts receiving escalating oral doses of 10, 20, 40, and 80 mg/kg body weight daily over a four-week period. At study conclusion, venous blood was obtained and serum concentrations of urea, creatinine, uric acid, sodium, and potassium were quantified as indices of renal integrity. Caffeine produced graded, dose-related changes in renal markers. Notably, urea, creatinine, and uric acid were all significantly elevated ($p < 0.05$) at the 40 mg/kg dose relative to vehicle-treated animals, pointing to a reduction in renal clearance capacity and glomerular filtration efficiency at higher exposures. Serum sodium and potassium, by contrast, were unaffected across all treatment levels ($p > 0.05$), indicating that electrolyte regulation remained intact throughout caffeine challenge. These results suggest that while substantial caffeine intake can compromise renal excretory function and disrupt nitrogenous waste handling, ionic homeostasis is preserved. Accordingly, moderate caffeine use appears physiologically tolerable, yet chronic or high-level consumption warrants careful consideration given its potential to impair kidney function.

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INTRODUCTION

Caffeine is a naturally occurring methylxanthine widely consumed across the world through coffee, tea, soft drinks, and energy beverages. Due to its central nervous system stimulant properties, caffeine is commonly used to enhance alertness and reduce fatigue. However, increasing consumption has raised concerns regarding its systemic effects, particularly on organs involved in metabolism and excretion.

The kidney plays a vital role in maintaining internal homeostasis by regulating fluid balance, electrolyte concentrations, and the excretion of metabolic waste products. Renal function is commonly assessed using biochemical markers such as serum urea, creatinine, and uric acid, which reflect the kidney's ability to filter and excrete nitrogenous wastes. Alterations in these markers are indicative of impaired renal function.

Caffeine has been reported to influence renal physiology through its diuretic action, adenosine receptor antagonism, and modulation of renal blood flow. These effects may alter glomerular filtration rate and tubular handling of solutes, potentially impacting renal function, especially with prolonged or high-dose exposure. Despite extensive consumption, experimental findings on the renal effects of caffeine remain inconsistent.

Electrolytes such as sodium and potassium are essential for maintaining osmotic balance, nerve conduction, and muscle function. The kidneys tightly regulate these electrolytes, and disturbances may lead to serious physiological consequences. Evaluating electrolyte balance alongside renal biomarkers provides a comprehensive assessment of kidney function.

Therefore, this study was designed to investigate the effects of caffeine administration on renal function biomarkers and electrolyte balance in male Wistar rats.

MATERIALS AND METHODS

Ethical Approval

All animal procedures were performed in full compliance with established international guidelines for the humane treatment and use of laboratory animals. Institutional ethical clearance was secured from the Animal Research Ethics Committee, Faculty of Basic Medical Sciences (details omitted for double-blind reviewing).

Location of Study

The study was conducted in the animal house of the Department of Human Physiology, Faculty of Basic Medical Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli Campus, Anambra State, Nigeria.

Materials

Twenty male Wistar rats, sawdust, Vital Top feed (grower and finisher), four standard rat cages, plates for feed and water, caffeine powder (25 g), electronic weighing balance, 2 mL syringe, oral cannula, measuring cylinder, capillary tube, examination gloves, cotton wool, chloroform, blood bottles, distilled water and centrifuge.

Experimental Design and Caffeine Administration

Twenty-five rats were randomly divided into five groups (n = 5 per group):
Group I (Control): Received distilled water only
Group II: Administered caffeine dissolved in distilled water at 10 mg/kg body weight daily (low dose)
Group III: Administered caffeine at 20 mg/kg body weight daily (medium dose)
Group IV: Administered caffeine at 40 mg/kg body weight daily (high dose)
Group V: Administered caffeine at 80 mg/kg body weight daily (highest dose)
Caffeine was dissolved in distilled water and administered orally once daily for the duration of the experimental period. The control group received an equivalent volume of distilled water.

Experimental Animals

Twenty-five healthy adult male Wistar rats weighing between 180 and 220 g were used for this study. The animals were obtained from the animal house of details omitted for double-blind reviewing. Rats were housed in well-ventilated cages under standard laboratory conditions (12-hour light/dark cycle, temperature 22–25 °C) and were provided with standard rat feed and clean drinking water ad libitum. The animals were acclimatized for two weeks prior to the commencement of the experiment.

Sample Collection

At the end of the experimental period, rats were fasted overnight and anaesthetized. Blood samples were collected via cardiac puncture into plain sample bottles. The blood samples were allowed to clot and then centrifuged at 3000 rpm for 10 minutes to obtain serum for biochemical analysis.

Assessment of Renal Function Biomarker

Serum urea was determined using the diacetyl monoxime method (Randox Laboratories, UK). Serum creatinine was measured by the Jaffe alkaline picrate reaction, and serum uric acid was quantified using the uricase-peroxidase colorimetric method, all performed according to the respective kit manufacturers' instructions.

Assessment of Serum Electrolytes

Serum sodium and potassium concentrations were measured using flame photometry (Jenway PFP7 Flame Photometer) according to standard operating procedures. Results were expressed in millimoles per litre (mmol/L).

Statistical Analysis

All results are reported as Mean ± Standard Error of Mean (SEM). Group differences in renal biomarker concentrations were evaluated by one-way analysis of variance (ANOVA); where a significant overall effect was detected, pairwise comparisons were performed using Tukey's Honest Significant Difference (HSD) post hoc test. A p-value of less than 0.05 was taken as the threshold for statistical significance throughout.

RESULTS

Effect of Caffeine Administration on Serum Urea Levels

Administration of caffeine resulted in a significant increase in serum urea levels compared with the control group ($p < 0.05$). The increase in urea concentration was dose-dependent, with higher caffeine doses producing progressively higher serum urea levels. Rats in the highest-dose group exhibited the greatest elevation in serum urea when compared with control animals (Table 1).

Effect of Caffeine Administration on Serum Creatinine Levels

Serum creatinine levels were significantly elevated in caffeine-treated rats compared with the control group ($p < 0.05$). The elevation in creatinine concentration followed a dose-dependent pattern, with increasing caffeine doses associated with higher creatinine levels. This finding suggests impaired renal filtration with increasing caffeine exposure (Table 2).

Effect of Caffeine Administration on Serum Uric Acid Levels

Serum uric acid concentrations were similarly elevated by caffeine in a dose-related fashion ($p < 0.05$ vs. control). The highest circulating uric acid values were recorded in the 80 mg/kg group, reinforcing the progressive nature of caffeine's impact on renal metabolite handling (Table 3).

Effect of Caffeine Administration on Serum Sodium Levels

Serum sodium concentrations did not vary significantly between caffeine-exposed animals and vehicle controls at any dose level ($p > 0.05$). Values remained tightly clustered across all experimental groups, demonstrating that oral caffeine at the doses employed had no measurable effect on sodium homeostasis (Table 5).

Effect of Caffeine Administration on Serum Potassium Levels

Similarly, serum potassium concentrations did not differ significantly between caffeine-treated groups and the control group ($p > 0.05$). Potassium levels remained relatively stable across all experimental groups, suggesting preserved potassium homeostasis despite caffeine exposure (Table 4).

Summary of Renal and Electrolyte Findings

Overall, caffeine administration caused significant, dose-dependent elevations in renal function biomarkers, including serum urea, creatinine, and uric acid, while serum electrolyte concentrations (sodium and potassium) remained largely unchanged.

Table 1: Effect of caffeine administration on serum urea level

Variable	Control (n=5)	Low Dose 10 mg/kg (n=5)	Medium Dose 20 mg/kg (n=5)	High Dose 40 mg/kg (n=5)	Highest Dose 80 mg/kg (n=5)
Urea (mg/dl)	28.40 ± 2.14	34.32 ± 2.89	33.01 ± 3.12	45.05 ± 3.76*	51.18 ± 4.23*
Post-hoc Pairwise Comparisons (Tukey HSD)	**Group Comparison**	**Mean Difference (I–J)**	**p-value (Sig.)**	**Interpretation**	
	Control vs Low dose	–5.92	0.779	Not significant	
	Control vs Medium dose	–4.61	0.864	Not significant	
	Control vs High dose	–16.65	0.016	Significant*	
	Low vs Medium dose	1.31	0.998	Not significant	
	Low vs High dose	–10.73	0.193	Not significant	
	Medium vs High dose	–12.04	0.136	Not significant	
Data expressed as Mean ± SEM. *p < 0.05 vs. Control (one-way ANOVA followed by Tukey's post hoc test).					

Table 2: Effect of caffeine administration on serum creatinine levels

Variable	Control (n=5)	Low Dose 10 mg/kg (n=5)	Medium Dose 20 mg/kg (n=5)	High Dose 40 mg/kg (n=5)	Highest Dose 80 mg/kg (n=5)
Creatinine (mg/dl)	0.68 ± 0.06	1.45 ± 0.14	1.31 ± 0.12	2.45 ± 0.22*	2.88 ± 0.27*
Post-hoc Pairwise Comparisons (Tukey HSD)	**Group Comparison**	**Mean Difference (I–J)**	**p-value (Sig.)**	**Interpretation**	
	Control vs Low dose	–0.77	0.098	Not significant	
	Control vs Medium dose	–0.63	0.188	Not significant	
	Control vs High dose	–1.77	0.006	Significant*	
	Low vs Medium dose	0.13	0.949	Not significant	
	Low vs High dose	–1.00	0.062	Not significant	
	Medium vs High dose	–1.13	0.041	Significant*	
Data expressed as Mean ± SEM. *p < 0.05 vs. Control (one-way ANOVA followed by Tukey's post hoc test).					

Table 3: Effect of caffeine administration on serum uric acid levels

Variable	Control (n=5)	Low Dose 10 mg/kg (n=5)	Medium Dose 20 mg/kg (n=5)	High Dose 40 mg/kg (n=5)	Highest Dose 80 mg/kg (n=5)
Uric Acid (mg/dl)	2.14 ± 0.31	4.37 ± 0.42	4.31 ± 0.38	6.31 ± 0.55*	7.42 ± 0.64*
Post-hoc Pairwise Comparisons (Tukey HSD)	**Group Comparison**	**Mean Difference (I–J)**	**p-value (Sig.)**	**Interpretation**	
	Control vs Low dose	–2.23	0.323	Not significant	
	Control vs Medium dose	–2.17	0.337	Not significant	
	Control vs High dose	–4.17	0.010	Significant*	
	Low vs Medium dose	0.06	1.000	Not significant	
	Low vs High dose	–1.94	0.389	Not significant	
	Medium vs High dose	–2.00	0.365	Not significant	
Data expressed as Mean ± SEM. *p < 0.05 vs. Control (one-way ANOVA followed by Tukey's post hoc test).					

Table 4: Effect of caffeine administration on serum potassium levels

Variable	Control (n=5)	Low Dose 10 mg/kg (n=5)	Medium Dose 20 mg/kg (n=5)	High Dose 40 mg/kg (n=5)	Highest Dose 80 mg/kg (n=5)
Potassium (mmol/L)	4.12 ± 0.18	4.25 ± 0.21	4.19 ± 0.19	4.31 ± 0.22	4.28 ± 0.20
Post-hoc Pairwise Comparisons (Tukey HSD)	**Group Comparison**	**Mean Difference (I–J)**	**p-value (Sig.)**	**Interpretation**	
	All pairwise comparisons	—	p > 0.05	Not significant	
Data expressed as Mean ± SEM. No significant differences detected across groups (one-way ANOVA, p > 0.05).					

Table 5: Effect of caffeine administration on serum sodium levels

Variable	Control (n=5)	Low Dose 10 mg/kg (n=5)	Medium Dose 20 mg/kg (n=5)	High Dose 40 mg/kg (n=5)	Highest Dose 80 mg/kg (n=5)
Sodium (mmol/L)	140.2 ± 1.84	141.6 ± 2.01	142.3 ± 1.97	143.1 ± 2.14	142.8 ± 1.92
Post-hoc Pairwise Comparisons (Tukey HSD)	**Group Comparison**	**Mean Difference (I–J)**	**p-value (Sig.)**	**Interpretation**	
	All pairwise comparisons	—	p > 0.05	Not significant	
Data expressed as Mean ± SEM. No significant differences detected across groups (one-way ANOVA, p > 0.05).					

DISCUSSION

This study evaluated the effects of caffeine administration on renal function biomarkers and electrolyte balance in male Wistar rats. The findings demonstrated that caffeine caused significant, dose-dependent elevations in serum urea, creatinine, and uric acid levels, while serum sodium and potassium concentrations remained largely unaffected. These results indicate that caffeine imposes functional stress on

the kidneys without markedly disrupting electrolyte homeostasis. All data were expressed as Mean ± Standard Error of Mean (SEM), and statistical comparisons were performed using one-way ANOVA followed by Tukey's post hoc test, with significance set at $p < 0.05$.

Serum urea and creatinine are established surrogate markers of renal excretory capacity, as both reflect the kidney's ability to clear nitrogenous end-products from the circulation. In the present study, serum urea levels increased progressively from a control value of 28.40 ± 2.14 mg/dl to 45.05 ± 3.76 mg/dl in the high-dose group (40 mg/kg), with the highest-dose group (80 mg/kg) recording 51.18 ± 4.23 mg/dl. Similarly, serum creatinine rose from 0.68 ± 0.06 mg/dl in controls to 2.45 ± 0.22 mg/dl and 2.88 ± 0.27 mg/dl in the high- and highest-dose groups, respectively. These significant elevations in urea and creatinine ($p < 0.05$) point to a reduction in glomerular clearance and possible tubular dysfunction. A plausible mechanistic explanation lies in caffeine's well-characterised role as an adenosine receptor antagonist: by blocking renal adenosine receptors, caffeine disrupts afferent arteriolar tone and alters intrarenal haemodynamics, thereby reducing effective filtration pressure and glomerular filtration rate, especially at elevated doses [1].

Uric acid is the final product of purine metabolism and is excreted primarily by the kidneys. In this study, serum uric acid levels increased from 2.14 ± 0.31 mg/dl in the control group to 6.31 ± 0.55 mg/dl and 7.42 ± 0.64 mg/dl in the high- and highest-dose groups, respectively. This significant dose-dependent elevation ($p < 0.05$) may indicate altered renal handling of urate or increased purine turnover. Elevated uric acid levels have been associated with renal dysfunction and increased oxidative stress, further supporting the notion of caffeine-induced renal strain [2].

Despite the observed alterations in renal biomarkers, serum sodium and potassium levels remained relatively stable across all treatment groups. Serum sodium ranged from 140.2 ± 1.84 mmol/L in controls to 143.1 ± 2.14 mmol/L in the high-dose group, while serum potassium ranged from 4.12 ± 0.18 mmol/L to 4.31 ± 0.22 mmol/L across groups. None of these differences reached statistical significance ($p > 0.05$). This suggests that the regulatory mechanisms responsible for electrolyte balance, including tubular reabsorption and hormonal control, were not significantly compromised by caffeine exposure within the study duration. Similar findings have been reported in experimental studies indicating that moderate renal stress may precede overt electrolyte disturbances [3].

The preservation of electrolyte balance alongside elevated renal biomarkers highlights an important distinction between functional renal stress and advanced renal failure. While caffeine appears to affect renal excretory function, compensatory mechanisms may maintain electrolyte homeostasis in the early stages of renal alteration. However, prolonged or excessive caffeine exposure may overwhelm these mechanisms, potentially leading to clinically relevant disturbances.

Overall, the findings of this study provide experimental evidence that caffeine administration can adversely affect renal function markers in a dose-dependent manner, underscoring the need for cautious consumption, particularly among individuals with pre-existing renal conditions.

Limitations of the Study

This study has several limitations that should be considered when interpreting the findings. First, the small group size ($n = 5$ per group) limits statistical power and the generalisability of results. Second, only male Wistar rats were used, and sex-related differences in caffeine metabolism and renal response cannot be excluded. Third, the study did not include histopathological examination of renal tissue, which would have provided direct structural evidence of caffeine-induced renal injury. Fourth, the experimental duration was fixed, and the long-term effects of prolonged caffeine exposure on renal function remain unknown. Finally, caffeine metabolism in rodents differs from that in humans, and results should be extrapolated to human populations with caution. Future studies should employ larger sample sizes, include both sexes, incorporate renal histology, and extend the observation period to better characterise the dose-response relationship.

CONCLUSION

Caffeine administration induces significant, dose-dependent increases in serum urea, creatinine, and uric acid levels in male Wistar rats, indicating altered renal function. In contrast, serum sodium and potassium concentrations remain largely unaffected, suggesting preservation of electrolyte balance. These findings indicate that caffeine may exert renal functional stress without causing overt electrolyte imbalance. Moderation in caffeine intake may therefore be important to minimize potential renal effects, especially in susceptible individuals.

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