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# Protective Effects of Cellgevity® Against High Fructose Diet-Induced Kidney Dysfunction and Hyperuricaemia in Wistar Rats

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ABSTRACT

**Background:** High fructose intake contributes to kidney dysfunction and elevated uric acid levels. Polyherbal supplements like Cellgevity® may offer protective benefits but have remained underexplored. This study evaluated the protective effect of Cellgevity® against kidney dysfunction and hyperuricaemia in rats fed a high-fructose diet.

**Materials and Methods:** Twenty male *Wistar* rats (180 - 220 g) were divided into four groups of five rats each: the control (normal diet), 60% High Fructose Diet (HFD) + 10% Fructose Water (FW), HFD+FW + Atorvastatin (3.52 mg/kg body weight), and HFD+FW + Cellgevity® (161.27 mg/kg body weight) groups. The feed and water were given *ad libitum,* while the Atorvastatin and Cellgevity® were dissolved in distilled water and administered using an oro-gastric gavage. After 28 experimental days, the rats were sacrificed and blood samples collected for estimation of electrolytes, urea, and creatinine and uric acid levels, using standard assay protocols. The results were analyzed by one-way ANOVA and Tukey's *post hoc* tests, using the Statistical Package for Social Sciences-20 software. Tissue histology of the rat's kidneys were also assessed.

**Results:** The HFD+FW group showed significantly higher ($P<0.05$) levels of urea (34.52±1.71), sodium (152.10±2.15) and uric acid (4.99±0.27) compared with the control group. Cellgevity® prevented significantly ($P<0.05$), these increases in urea (25.74±0.82), sodium (138.90±1.10), and uric acid (1.16±0.28). The HFD caused focal tubular necrosis, interstitial congestion, interstitial infiltrates of inflammatory cells, in the kidneys of the rats, while Cellgevity® protected the kidneys against such changes.

**Conclusion:** Cellgevity® demonstrated promise in protecting against high-fructose diet-induced renal dysfunction and hyperuricaemia in *Wistar* rats.

**Keywords:** High fructose diet, Cellgevity®, Urea, Electrolytes, Hyperuricaemia

## INTRODUCTION

In recent decades, the global burden of chronic metabolic disorders, including obesity, hypertension, diabetes mellitus, and chronic kidney disease (CKD), has escalated in parallel with a significant increase in dietary consumption of fructose, particularly in the form of high-fructose corn syrup (HFCS) used in sweetened beverages and processed foods. Fructose, unlike glucose, is metabolized primarily in the liver through a unique and unregulated pathway (1). This metabolic route involves its rapid phosphorylation by fructokinase to form fructose-1-phosphate, bypassing the regulatory enzyme phosphofructokinase (1). This process leads to a sudden depletion of intracellular ATP and inorganic phosphate, triggering the degradation of AMP to inosine monophosphate and eventually to uric acid via the xanthine oxidase pathway (1).

The resultant increase in uric acid production contributes to hyperuricaemia, which is not merely a by-product of purine metabolism but an active participant in the pathogenesis of various metabolic and renal diseases (1). Elevated uric acid levels have been implicated in endothelial dysfunction through the reduction of nitric oxide bioavailability, leading to vasoconstriction, oxidative stress, and inflammation within the renal microvasculature (2). Additionally, uric acid induces the activation of the renin-angiotensin system (RAS), further exacerbating hypertension and renal injury by promoting sodium retention and fibrotic changes in renal tissues (3).

Fructose intake also stimulates de novo lipogenesis and increases intracellular lipid accumulation, which may impair mitochondrial function and enhance the generation of reactive oxygen species (ROS) (4). Both fructose and uric acid upregulate pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), as well as transforming growth factor-beta (TGF-β), which collectively contribute to renal inflammation, tubular damage, and progressive tubulointerstitial fibrosis (4). These pathological changes compromise glomerular filtration, tubular reabsorption, and overall nephron integrity, ultimately

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culminating in kidney dysfunction (4). Furthermore, studies have demonstrated that high-fructose diets not only elevate serum uric acid but also reduce urinary excretion of uric acid by down regulating transporters like Uric Acid Transporter 1 (URAT1) and Glucose Transporter 9 (GLUT9) in renal tubular cells, thereby aggravating hyperuricaemia (5).

The central role of dyslipidaemia and oxidative stress in fructose-induced metabolic and renal disorders has positioned antidyslipidaemic and antioxidant therapy as a promising avenue for intervention (6). Glutathione (GSH), the most abundant intracellular antioxidant, plays a crucial role in cellular defense against oxidative damage by neutralizing free radicals and maintaining redox balance (6). However, excessive ROS production, as seen in high-fructose conditions, rapidly depletes intracellular GSH stores, leaving tissues vulnerable to oxidative injury (6).

Atorvastatin, a drug with antihyperlipidaemic and renoprotective properties (7, 8, 9), was chosen as the standard reference drug for this study, because it has been established that the aetiopathogenesis of the anomalies caused by a high fructose diet is majorly the direct consequence of the dyslipidaemia (increased in blood free fatty acids, hypercholesterolaemia and hypertriglyceridaemia) that it induces (10).

The manufacturers of Cellgevity®, a polyherbal dietary supplement developed by Max International, USA, claim that it has protective effects against cardio-metabolic diseases and organ damage (12). It is said to enhance the endogenous production of glutathione through its key component, RiboCeine™—a compound consisting of D-ribose and L-cysteine (11). RiboCeine™ is said to facilitate efficient cysteine delivery, the rate-limiting precursor in glutathione biosynthesis (11). In addition, Cellgevity® also contains a blend of biomolecules and herbal extracts with known antilipidaemic, antihypertensive, antioxidant and anti-inflammatory properties (12). They include alpha-lipoic acid, resveratrol, curcumin, quercetin, milk thistle extract, and selenium (12). *In-vivo* studies on the serum of Wistar rats, fed a high fructose diet shows that Cellgevity® has the potential to attenuate the inflammation and oxidative stress induced by high fructose intake (12). Despite the claims on its therapeutic benefits, there is paucity of scientific data evaluating the efficacy of Cellgevity® in mitigating organ-specific pathologies, particularly those on the kidneys, induced by metabolic derangements caused high-fructose intake. Given the claims on the therapeutic benefits of Cellgevity® and the multifactorial mechanisms underlying fructose-induced renal dysfunction and hyperuricaemia—ranging from the effect of fructose induced dyslipidaemia, ATP depletion and uric acid accumulation to activation of oxidative stress and inflammation (1, 2, 3, 4, 5), there is a strong rationale to investigate whether Cellgevity® can confer renoprotective benefits when given together with a renotoxic diet like a high fructose diet.

This study, therefore, explored the protective effects of Cellgevity® against high-fructose diet-induced kidney dysfunction and hyperuricaemia in *Wistar* rats. The outcome of this research may provide insights into the therapeutic potential of Cellgevity® in protecting or attenuating fructose-related renal and metabolic disorders.

## MATERIALS AND METHODS

### Ethical Approval

Ethical approval was obtained from the Research Ethics Committee (REC) of the College of Medical Sciences, University of Benin, with approval Number: CMS/REC/2023/485.

### Materials and Reagents

Cellgevity® was bought from Max international (USA), while Atorvastatin manufactured by TEVA UK limited, was procured from a pharmaceutical outlet, Thelver Pharmacy, Ugbowo, Benin-Lagos Expressway, Benin City, Edo State, Nigeria. The pure white crystalline powdered D (-) Fructose by Loba Chemie PVT Limited, India, was purchased from a reagent store, Emytex Biomedicals Ugbowo, Benin-Lagos Expressway, Benin City, Edo State. Kidney function tests conducted in this study, except for electrolyte assessments (which were performed using an ion-selective electrode device), utilized diagnostic kits supplied by Randox Laboratories, UK, containing the following reagents EDTA, sodium nitroprusside, and urease enzyme; diluted phenol; and diluted sodium hypochlorite. Others were sodium hydroxide, standard urea solution, and picric acid. All assays were carried out in accordance with the manufacturer's protocols to ensure accurate and reliable determination of renal function parameters.

### Experimental Animals

Male Wistar rats (n=20) weighing between 180g and 220g were acquired from the Anatomy Department, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria. These rats were acclimatized for two weeks, adhering to international guidelines as recommended by the Canadian Council on Animal Care (13).

### Experimental Diets

The experimental procedure involved the administration of a basal diet, comprising standard pelleted growers mash (Table 1) and a high-fructose diet (HFD) known to induce kidney dysfunction and hyperuricaemia as part of its metabolic syndrome inducing effects (Table 2), consumed *ad libitum*. This high-fructose diet was formulated by supplementing a proportional quantity of the basal diet with white crystalline powdered D (-) Fructose, resulting in a diet with a 60%

fructose content (14). This diet was supported by allowing the rats to drink *ad libitum*, 10% fructose water (FW) (15).

**Table 1: Composition of the basal diet (g/1000g) based on of the standard pelleted growers mash of Jerrison Agro Allied Services, Benin City, Nigeria**

| Ingredients | Basal diet (g) |
|---|---|
| Maize | 280 |
| Wheat Offal | 280 |
| Palm Kernel Cake | 208 |
| Soyabean Meal | 48 |
| Groundnut Cake | 100 |
| Fish Meal (65%) | 12 |
| Lysine | 1.6 |
| Bone Meal | 12 |
| Limestone | 52 |
| Methionine | 0.8 |
| Grower Premix | 2.4 |
| Salt | 3.2 |
| **Total** | **1000** |

**Table 2: Composition of the 60% high fructose diet (metabolic syndrome-inducing diet) (g/1000g)**

| Ingredients | High-Fructose Diet (g) |
|---|---|
| Basal diet in Table 1 | 400 |
| Pure white crystalline powdered Fructose | 600 |
| **Total** | **1000** |

**Experimental Design**

For this study, the animals were randomly divided into four groups, each serving a specific purpose:

Group 1: Received a basal diet with clean tap water (control group) *ad libitum*

Group 2: Given a 60% fructose diet (HFD) along with 10% fructose-water (FW) *ad libitum*

Group 3: Given a 60% fructose diet, 10% fructose-water, (*ad libitum)* and Atorvastatin (4.13 mg/kg-body weight), (orally, using an oro-gastric gavage)

Group 4: Given a 60% fructose diet, 10% fructose-water, (*ad libitum)* and Cellgevity® (161.27 mg/kg-body weight), (orally, using an oro-gastric gavage).

**Dosage Regimen**

The dose of the Atorvastatin and Cellgevity® used, were derived from the rat equivalent of the dose already recommended for humans, taking cognizance of the weight of each rat (12, 16).

**For Cellgevity®:** The manufacturers recommended human oral dose is 2 capsules daily, which amounts to 26.15 mg/kg used for this study (12). To get the equivalent quantity of the Cellgevity® needed to be administered to the rats, the powdery-content of the Cellgevity® capsules, were removed and weighed using a weighing scale. To convert the recommended human dose to an appropriate rat equivalent dose (RED), body surface area normalization was employed using the FDA-recommended Km values for dose translation (16):

RED (ml/kg) = Human dose × (Km human / Km rat)

RED = 26.15 mg/kg × (37 / 6) ≈ 161.27 mg/kg

This rat-equivalent dose of 161.27 mg/kg was therefore used for this study.

**For Atorvastatin**: The manufacturers recommended human oral dose is 40mg daily, which amounts to is 0.67 mg/kg (12). To convert this to an appropriate rat equivalent dose (RED), body surface area normalization was employed using the FDA-recommended Km values for dose translation (16):

RED (mg/kg) = Human dose × (Km human / Km rat)

RED = 0.67 mg/kg × (37 / 6) ≈ 4.13 mg/kg

This rat-equivalent dose 4.13 mg/kg was therefore used for this study.

**The Feeding Protocol**

With *ad libitum* access to the feeds (basal and experimental diets), the animals' daily intake was closely monitored throughout the four-week study period. Cages were managed within a 12-hour light-dark cycle, and regular cleaning and disinfection procedures were implemented to maintain a hygienic environment. Cellgevity® and the Atorvastatin drug were administered orally.

**Blood Sample Collection**

Blood samples were obtained on the 29th day, after the 28-day experimental period. This was after an overnight fast and under chloroform anesthesia, through cardiac puncture. The samples were put into lithium heparin bottles, which were also later centrifuged at 4000r/min for 10mins to obtain plasma. Their plasma supernatants were separated into sterile plain bottles and used for the evaluation of kidney function status and serum uric acid levels of the rats.

**Plasma Electrolytes ($Na^+$, $K^+$, $Cl^-$, $HCO_3^-$):** Plasma concentrations of sodium, potassium, chloride, and bicarbonate were determined using an ion-selective electrode (ISE) analyzer based on the method described by Tietz *et al.* (17). The system measures electrical potentials generated by specific ion-selective membranes, and concentrations were calculated automatically using the Nernst equation after calibration with standard solutions.

**Plasma Urea:** Urea concentration was estimated using the urease–phenol–hypochlorite method (18) as described by the manufactures of the kit, Randox (UK), used for its estimation. Urea was hydrolyzed to ammonia and carbon dioxide; the ammonia formed reacted with phenol and hypochlorite to produce a blue indophenol complex. Absorbance was measured at 546 nm and compared to a standard urea solution, to determine concentration.

**Plasma Creatinine:** Creatinine was measured using the Jaffe reaction (19) with a Randox kit. In this method, creatinine reacts with picric acid in an alkaline medium to form a colored complex. Absorbance was recorded at 492 nm, and concentration was determined based on the change in absorbance over a two-minute interval, using a standard curve.

**Uric Acid:** Uric acid is measured using an enzymatic colorimetric method where uricase oxidizes uric acid to produce hydrogen peroxide, which reacts with a chromogen to form a colored compound. The color intensity, measured at 500–520 nm, is proportional to the uric acid concentration. (20)

**Kidney Tissue Collection and histological evaluation**

After blood was collected from the anaesthesized rats, the kidney tissues were harvested and fixed in a 10% formal-saline solution. After fixation, samples were dehydrated in ascending alcohol series and embedded in paraffin wax in order to be stained by hematoxylin and eosin and examined under light microscopy (at 400× magnification) for histopathological study based on Kiernan protocol (21). A histopathologist reviewed slides blindly. Microscopic features of renal tissue were considered and histological changes for each case was photographed and recorded.

**Statistical Analysis**

The assessment of statistical significance was conducted using Analysis of Variance and the Tukey's *post hoc* test, at a 95% confidence level, employing the Statistical Package for Social Sciences-20 software. Results with $P < 0.05$ were considered significant.

## RESULTS

The high fructose diet (HFD) + 10% fructose water (FW) induced a significant increase ($p < 0.05$) in urea levels in the rats compared to the control group (Table 3). In contrast, Atorvastatin and Cellgevity® demonstrated significant efficacy in mitigating this rise in urea levels ($p < 0.05$), effectively maintaining levels akin to the control group (Table 3).

The high fructose diet and 10% fructose water caused no significant difference ($p>0.05$) in Creatinine, Potassium, Chloride and Bicarbonate levels in the rats when compared with the control group and with the other experimental groups respectively (Table 3 and 4).

The high fructose diet and 10% fructose water however caused a significant increase ($p<0.05$) in sodium and uric acid levels in the rats when compared with the control group (Table 4 and 5). Generally, Atorvastatin and Cellgevity® significantly ($p<0.05$) prevented in their respective groups, these increases observed in the HFD control group, with Cellgevity® observed to have significantly ($p<0.05$) more effect in preventing the rise in sodium levels in the rats when compared to the effect of Atorvastatin.

**Table 3: Urea and Creatinine levels of the rats fed high-fructose diet and 10% fructose water**

| Groups | Urea (mg/dl) | Creatinine (mg/dl) |
|---|---|---|
| Group 1 (Control) | 23.72±0.85[a] | 1.07±0.11[a] |
| Group 2 (HFD+FW) | 34.52±1.71[b] | 1.04±0.15[a,] |
| Group 3 (HFD+FW + Atorvastatin) | 27.60±1.03[a] | 0.94±0.10[a] |
| Group 4 (HFD+FW + Cellgevity®) | 25.74±0.82[a] | 1.05±0.13[a] |

The results were expressed as mean ± SEM (= standard error of the mean). Means with different superscripts differ significantly from one another at 95% level of significance (*P < 0.05*). **HFD+FW:** High fructose diet + fructose water

**Table 4: Electrolytes levels of the rats fed high-fructose diet and 10% fructose water**

| Groups | Sodium (mmol/l) | Potassium (mmol/l) | Chloride (mmol/l) | Bicarbonate (mmol/l) |
|---|---|---|---|---|
| Group 1 (Control) | 132.10±1.31[a] | 3.33±0.21[a] | 100.20±1.48[a] | 17.34±3.72[a] |
| Group 2 (HFD+FW) | 152.10±2.15[b] | 3.60±0.28[a] | 102.60±1.39[a] | 17.90±0.49[a] |
| Group 3 (HFD+FW+ Atorvastatin) | 140.60±1.69[b] | 4.16±0.35[a] | 103.30±0.73[a] | 16.41±1.30[a] |
| Group 4 (HFD+FW+ Cellgevity®) | 138.90±1.10[a] | 3.83±0.12[a] | 98.44±0.79[a] | 16.46±0.40[a] |

The results were expressed as mean ± SEM (= standard error of the mean). Means with different superscripts differ significantly from one another at 95% level of significance (*P < 0.05*). **HFD+FW:** High fructose diet + fructose water

**Table 5: Uric acid levels of the rats fed high-fructose diet and 10% fructose water**

| Groups | Uric Acid (mg/dl) |
|---|---|
| Group 1 (Control) | 2.65±0.06[a] |
| Group 2 (HFD+FW) | 4.99±0.27[b] |
| Group 3 (HFD+FW + Atorvastatin) | 2.21±0.20[a] |
| Group 4 (HFD+FW + Cellgevity®) | 1.16±0.28[c] |

The results were expressed as mean ± SEM (= standard error of the mean). Means with different superscripts differ significantly from one another at 95% level of significance (*P < 0.05*). **HFD+FW:** High fructose diet + fructose water

As depicted in Plate 1, the kidney tissue of control rats exhibits a normal tissue architecture with the tubules (TU), glomeruli (GL) and interstitial space (IS) all appearing normal and unremarkable. In Plate 2, the kidney tissue of rat given high fructose diet + 10% fructose-water shows loss of renal integrity indicated by presence of focal tubular necrosis (TN),

interstitial congestion (CO) and interstitial infiltrates of inflammatory cells (IC). The observations from Plate 3 indicate that when Cellgevity is administered alongside the experimental diet, it mitigates the adverse impacts of the high fructose diet and 10% fructose water. Specifically, the kidney's glomerular architecture (GL) and the tubules (TU) remains unaffected and appears normal. The observations from Plate 4 indicate that like Cellgevity®, when Atorvastatin is administered alongside the high fructose diet and 10% fructose water, it also mitigates the adverse impacts of the high fructose diet and 10% fructose water, as the kidney's glomerular architecture (GL) and Tubules (TU) remains unaffected and appears normal.

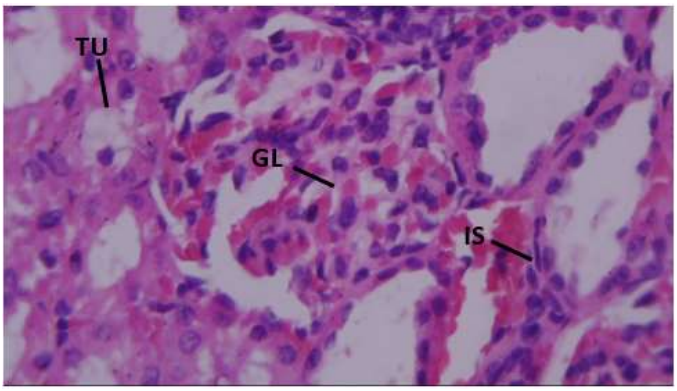



Plate 1: Rat kidney (Control). Composed of normal tissue architecture: tubules (TU), glomeruli (GL), interstitial space (IS): H&E; 400x

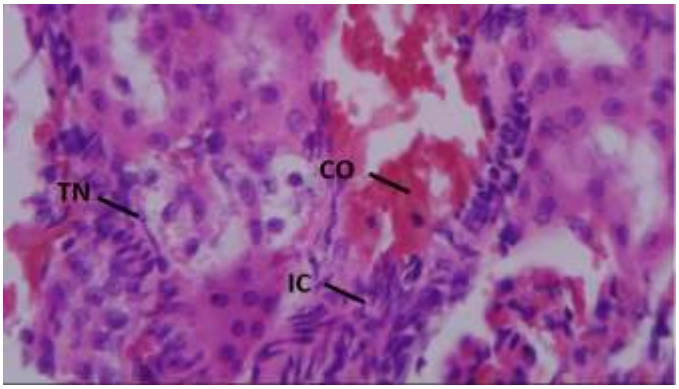



Plate 2: Rat kidney given high Fructose diet + 10% Fructose-water, showing focal tubular necrosis (TN), interstitial congestion (CO), interstitial infiltrates of inflammatory cells (IC): H&E; 400x.

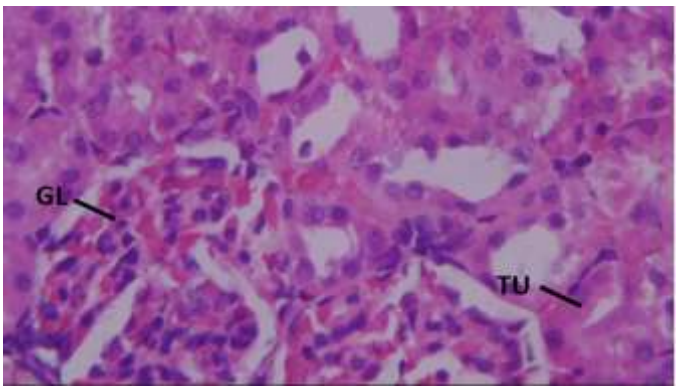



Plate 3: Rat kidney given high Fructose diet + 10% Fructose-water + Cellgevity, showing normal tubules (TU), normal glomeruli (GL): H&E; 400x

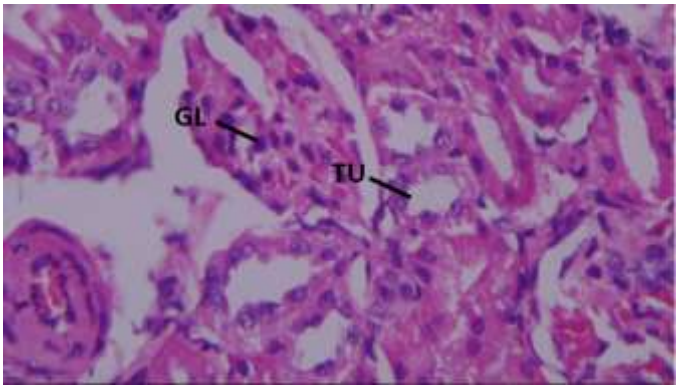



Plate 4: Rat kidney given high Fructose diet + 10% Fructose-water + Atorvastatin, showing: normal glomeruli (GL), normal tubules (TU): H&E; 400x.

## DISCUSSION

This study explored the protective effects of Cellgevity® against kidney dysfunction and hyperuricemia induced by a high-fructose diet combined with 10% fructose water (HFD+FW). The findings provide insight into the biochemical and histopathological consequences of excessive fructose consumption and the mitigating potential of Cellgevity®, a supplement containing riboceine—a precursor to glutathione known for its antioxidant properties (1).

The HFD+FW group showed a significant elevation in urea levels compared to the normal control group ($p < 0.05$), which aligns with previous findings (22), where it was reported that high dietary fructose increases serum urea and may impair nitrogen metabolism (22). Urea, a product of protein catabolism, reflects the level of kidney function efficiency as it is primarily excreted via the renal system (22). The observed increase may indicate early renal stress, protein metabolism alterations, or dehydration-related effects due to hyperglycemia-induced osmotic diuresis (23). Elevated urea levels in the context of high fructose intake may also result from increased purine metabolism and hepatic stress, leading to impaired nitrogen excretion (22). Interestingly, intervention with Atorvastatin and Cellgevity® significantly attenuated this urea increase ($p < 0.05$), maintaining levels similar to the control group. This suggests renoprotective effects of atorvastatin at play (7, 8, 9), and the renoprotective effect of Cellgevity, potentially attributable to its antioxidant and anti-inflammatory properties (12) and the renoprotective properties of its constituent phytochemicals from the herbal extracts they contain (12, 24, 25). Cellgevity®, by boosting intracellular glutathione, likely prevented oxidative damage to renal cells, thereby preserving their excretory function.

Creatinine levels remained statistically unchanged across all groups, indicating that any overt renal failure or glomerular filtration rate compromise has not yet reached a severe level. Although creatinine is a key renal biomarker, it often remains stable until significant nephron loss has occurred. The stability in potassium, chloride, and bicarbonate levels further suggests the preserved electrolyte regulatory functions of the kidneys,

despite the metabolic stress induced by the HFD+FW regimen. The findings also infer that Cellgevity® maintained the status quo of the renal function, which points towards a conclusion that it is not renotoxic.

However, sodium levels significantly increased in the HFD+FW group ($p < 0.05$), suggesting possible sodium retention or reduced renal sodium excretion. Elevated sodium may be related to fructose-induced activation of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system stimulation (26). Such dysregulation could promote hypertension and further renal injury if left unchecked. Treatment with Atorvastatin and Cellgevity® significantly prevented sodium levels ($p < 0.05$) from rising. This suggests that Cellgevity® may help prevent unnecessary sodium reabsorption and enhance natriuretic processes that keep sodium at a normal level, further highlighting its nephroprotective capability.

Perhaps the most striking finding is the marked increase in uric acid in the HFD+FW group ($p < 0.05$), supporting evidence that fructose metabolism bypasses key glycolytic regulation, leading to ATP depletion, increased AMP breakdown, and subsequent uric acid production (1, 26). Hyperuricaemia is a known contributor to renal vasoconstriction, inflammation, and crystal deposition, all of which can exacerbate kidney injury (27). Remarkably, Cellgevity® significantly ($P<0.05$) reduced uric acid levels below that of the normal control group, outperforming Atorvastatin. This finding suggests that the phytochemical constituents of Cellgevity® that prevents fructose induced dyslipidaemia, along with its constituents that have glutathione-increasing antioxidant abilities, may have enhanced the uricosuric action or urate-lowering potential of Cellgevity®, potentially via glutathione-mediated inhibition of xanthine oxidase activity or improved renal uric acid clearance. These results align with prior studies indicating that oxidative stress inhibition can reduce uric acid synthesis (24, 28).

Histological examination further substantiates the biochemical data. In HFD+FW rats, kidney tissues exhibited focal tubular necrosis, interstitial congestion, and infiltration of inflammatory cells, indicating nephrotoxicity and compromised renal architecture. These alterations are consistent with previous reports on fructose-induced kidney damage (29). In contrast, Cellgevity® -treated rats displayed largely preserved glomerular structures, with normal glomerulus and tubules and no significant inflammation. This supports the idea that Cellgevity® confers structural renoprotection, likely through antioxidative and anti-inflammatory pathways. Comparatively, Atorvastatin also preserved glomerular integrity, implying that Cellgevity® may offer similar comprehensive nephroprotection.

The therapeutic efficacy of Cellgevity® apart from the beneficial effects of its active biomolecules and phytochemicals, can be linked to its active ingredient—Riboceine, a compound that facilitates glutathione synthesis within cells (12). Glutathione is a potent intracellular antioxidant that combats oxidative stress, a major driver of fructose-induced renal injury (30). Earlier studies have shown that Cellgevity® prevents the progression of the deleterious effect of a high fructose diet by preventing the onset of oxidative stress and inflammation (12). By replenishing glutathione, Cellgevity® may inhibit pro-oxidant pathways (12), stabilize mitochondrial function, and prevent uric acid overproduction. In contrast, Atorvastatin's benefits are largely attributed to its anti-inflammatory and endothelial-protective actions (31) which, while effective, may not counteract oxidative stress as robustly as the glutathione-boosting strategies of Cellgevity® (12).

**Conclusion:** In summary, a high-fructose diet induced significant metabolic disturbances including hyperuricaemia, elevated urea, and sodium deregulation, with corresponding histopathological kidney damage. Cellgevity® demonstrated superior protective effects, normalizing biochemical parameters and preserving renal histoarchitecture more effectively than Atorvastatin. These findings highlight that the co-administration of the supplement Cellgevity®' may have the potential of preventing high fructose-diet related renal dysfunction and hyperuricemia.

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